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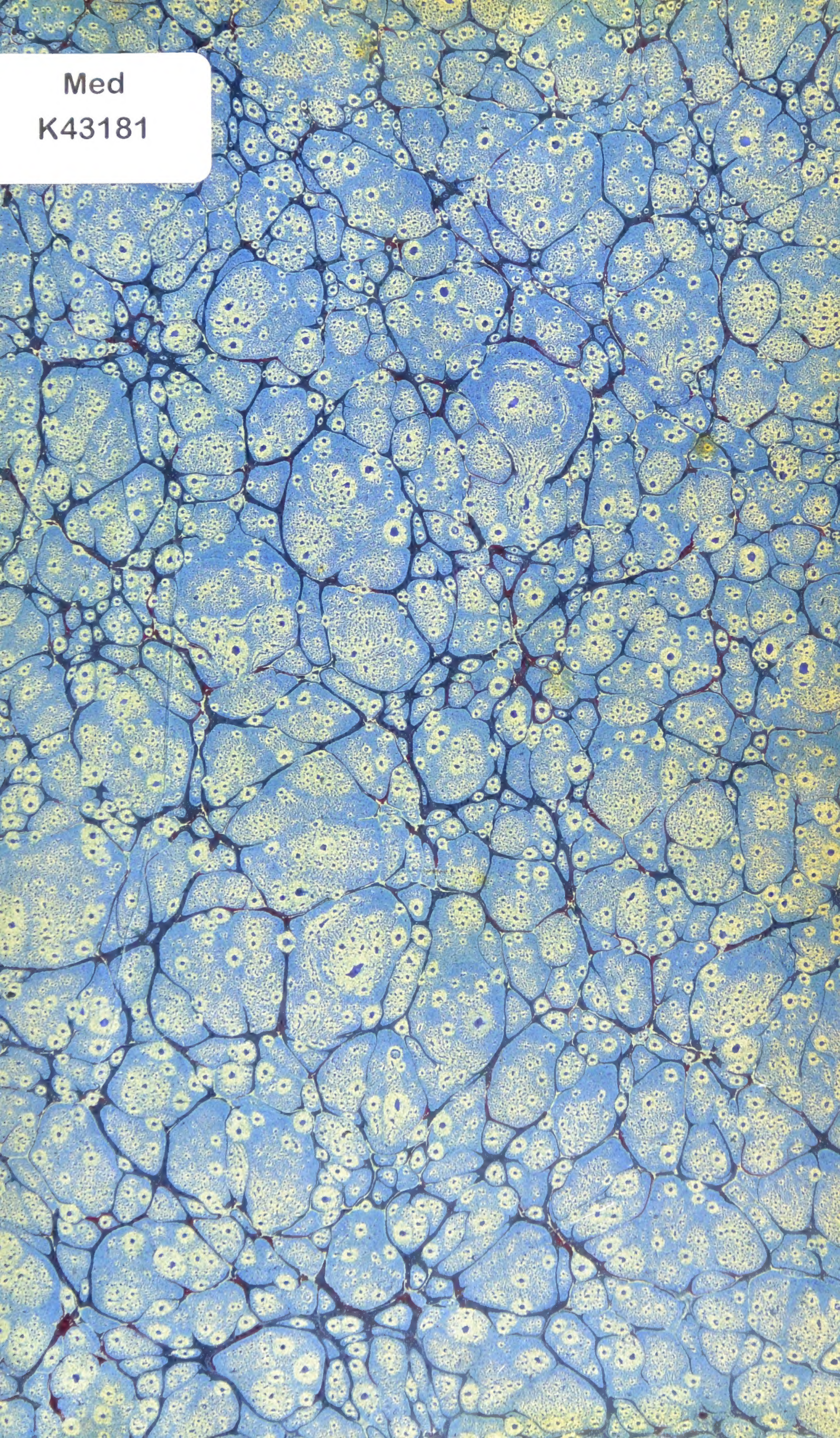

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SURGERY

ITS PRINCIPLES AND PRACTICE

BY VARIOUS AUTHORS

EDITED BY

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VOLUME I

With 261 Text-Illustrations and 17 Colored Plates

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PREFACE

When the W. B. Saunders Company urged me to undertake the editorship of so formidable a work as a Surgery comprising five volumes and over 4000 pages, I was very loth to do so. But though its organization has involved a great deal of labor, it has brought me into intimate and continual contact with nearly four-score of the brightest, most ardent, and earnest surgical scholars and experts of Europe and America, and has proved a daily stimulus and pleasure. Their coöperation has been constant, hearty, and helpful, and I gladly recognize its value.

It has been our aim to record the very latest well established knowledge so that the work should be thoroughly "up to date," yet with few, if any, passing surgical novelties.

My thanks are especially due to Professor J. Chalmers Da Costa, whose ripe surgical knowledge, advice, and practical aid have been and will continue to be of inestimable value.

That the publishers have given generous help, this volume is the best evidence. They have cheerfully coöperated from the very first, and have spared no expense, especially in the many illustrations.

The other four volumes will follow as rapidly as they can be printed.

If the joint work of authors and editor, onerous as it has been, shall contribute to the increase and diffusion of the knowledge of surgery, so that our colleagues of the profession and we ourselves may be better equipped for the prevention, the care, and the cure of surgical ills, the diminution of suffering, the prolongation of life, and the increase of happiness of the human race, our best and highest wishes and hopes will be more than fulfilled.

William W. Keen.

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SURGERY

KEEN

SURGERY

ITS PRINCIPLES AND PRACTICE.

CHAPTER I.

NARRATIVE OF SURGERY; A HISTORICAL SKETCH.

By James Gregory Mumford, M.D.,

BOSTON.

"*Ut transeundi spes non sit, magna tamen est dignitas subsequendi.*"—Quintilian.

HIPPOCRATES.

470 to 361 B. C.

Hercules was the father of Æsculapius, who was the father of Polidarius (one of Homer's heroes), and so on for twelve generations until we come to the first Hippocrates, who was the grandfather of the second Hippocrates, the *Great Hippocrates*, born about 470 B. C. Much of this genealogy is myth, but there is no myth about Hippocrates. He was a man.

Among medical heroes it is the positive, the virile, the real, that appeals to us. Mists and vapors, hypotheses and systems, do not interest the average modern reader; but things accomplished and the final word said, do interest him. So observe this, that deeds done, facts accurately stated, action taken in accordance with what is known,—these things are characteristic of the history of surgery as distinguished from much of the history of medicine. Often we cannot divorce the two tales of medicine and surgery, but very often we can; and when this is possible, the tale of surgery and of the surgeon will attract us.

Hippocrates was the Father of Medicine, but he was a surgeon also; Herophilus after him was a surgeon; so were Asclepiades and Soranus and Galen and Paul of Ægina, and others of whom the writers tell.

Who was this famous Hippocrates? Where did he live? What were his teachings, and who his professional forebears? What was it he did that he is to be remembered as the father of us all?

Hippocrates was born and lived in stirring times. His native place was the Greek island of Cos, close to the coast of Asia Minor, and in about the latitude of Sparta. In those days the tide of Persian invasion was being rolled back; the Athenians, under Cimon, were re-establishing Greek supremacy in the Levant, on the eastern shores of the Ægean

Sea, and Athens was developing that era of social and intellectual greatness to which we now refer as the Age of Pericles—an era covered roughly by the sixty years subsequent to the battle of Salamis (480 B. C.).

Hippocrates grew up in an island Athenian in its sympathies and affiliations; and the influence lasted throughout his life. He came of a family of physicians, long trained in a medical practice handed down from father to son; and be it observed that medical practice was not altogether contemptible even before his time. For more than a thousand years the surgery of Egypt had meant something to the world, and the ancient Egyptian custom of embalming the dead had given its practitioners a little crude knowledge of anatomy. They trephined the skull for migraine and epilepsy, they performed circumcision, they removed superficial tumors, and they set broken bones.

Then there were the Old Testament Jews, who made acquaintance with surgery, an acquaintance acquired from their Egyptian masters. They sutured wounds and passed the uterine sound; they appear to have operated for imperforate anus and are said to have used some feeble anesthetics. There were dentists among them who inserted false teeth, and there were artificers of wooden legs. Such accomplishments show very practical advances in surgery, many centuries before our era.

Egyptian surgeons became famous; they traveled and visited foreign courts and peoples, practising upon the bodies of Arabians, Persians, Assyrians, and Greeks. Nor were the Greeks themselves idle through all those years. In some sort they were the Yankees of that far-away ancient world. They were travelers, traders, seamen, and scholars,—always restless, eager, inquisitive; seeking new markets, planting colonies, looking for knowledge.

It came about, then, long before Hippocrates was born, while Æsculapius was being deified and Polidarius was quoted still, that much of the Egyptian learning was beginning to find its way to the Greek mainland and to the islands of the sea. Surgeons were esteemed in that Greek country of intelligent men, for the people were warlike, and even in the days of Homeric heroes there was honor for those who healed the wounded. A little later one learns of Æsculapian families (Asclepiadæ) settled, and of their establishing medical schools, or systems of healing, in various parts of the Greek world; whether or not they were descendants of Æsculapius matters nothing now; but, mark you, these men were physicians and surgeons, not priests; though priests of the temples of Æsculapius did come to occupy an important place in the thoughts of the people.

So the profession of medicine became hereditary in certain families. The practitioners lived together in little communities, to which patients went for treatment. In these communities schools grew up and records were kept; experience accumulated; knowledge was transmitted from generation to generation. The young men were educated carefully and broadly; they were general practitioners as well as specialists; now and again a promising lad was sent abroad to complete his studies. He went to Athens, to Rhodes, to Cyrene, to Cnidos, to Cos; through Syria, Persia, Egypt. He traveled on foot or by ship; studying the peoples and the languages, visiting famous men and famous places. He inspected clinics, he followed special forms of treatment; often he tarried long. Such a man might spend years, or a lifetime, even, in acquiring special knowledge or in broadening his general culture. Betimes he was tempted by a handsome offer from some foreign ruler or great man to stay with him and practise. Great surgeons of those days were known to pass their lives in such professional adventures; in settling and studying and practising and moving on, consumed always by a restless craving for new knowledge. There must have been a fascination about it, and in those days when your neighbor-city was a month's journey distant, when language changed with every hamlet, when information traveled at a foot-pace and news was news still for a decade, one may fancy the delight of moving on and on, leisurely learning things and doing things. The knowledge thus gained was brought back to the home schools, in greater or less amount, and those schools became dêpots for the learning of the day. So it is probable that before Hippocrates, a good part of the surgical acquirements of earlier times had been collected in his family school in Cos. The fifty years preceding his birth were active years with men. There had come a sudden rush of expansion among the Greeks to the west; and the Persians to the east were extending their boundaries and rolling forward to the Mediterranean those vast armies and armadas which the Greeks crushed at Platæa, Salamis, and Mycalé. There was extensive experience of military surgery, and the surgeons of Cos doubtless saw their share. Records of such things, fragmentary, unsystematized, but abundant, were accumulating.

It was into this world and to such a life that Hippocrates was born. He was the prophet needed to give articulate expression to that formless learning, to show the meaning of what other men had seen, and out of his own wide experience to add the master-word of the great teacher. Fain would one know more of his life. We glean scattered fragments from the old writers; there are letters and gossip and tradition, but no connected tale. He grew up and studied his profession in Cos; then he set out on his travels. There is an old lie about his reason for leaving home—a lie often refuted; his detractors used to say that he owed a great part of his knowledge to the famous library in Cnidos, a promontory of the mainland about twelve miles south of Cos; that after he had extracted from the library all he could, he burned it down so as to balk all future students; and that then he ran away. At any rate, he traveled in many lands, returning at times to his native place for rest and further teaching. How far his wanderings took him does not appear, but mostly he lived and practised in sundry places on the Greek mainland, as well as in that country latterly called Turkey in Europe; we hear of him in Athens, Delos, Thessaly, and Thrace. During his journeyings he married and had several children. Two sons, Thessalus and Draco, are known to us, and each of them had a son Hippocrates. All were physicians, calling Cos their home. A daughter of our Hippocrates married Polybus, in his turn a celebrated physician. Hippocrates spent many of his best years, youth and age, in Thessaly and Macedonia. Thessaly was his first abiding-place after he left home, and he became widely known while living at Larissa. They tell a story about him in this period: Perdicas was a young king of the neighboring country of Macedonia. For many months he had been thought to have consumption; at last, taking counsel with wise men, he sent to Larissa for Hippocrates to cure him. That shrewd physician quickly convinced himself that the king was a timid lad, hopelessly in love; "Nor in this was he mistaken," as the chronicler says,[*] "for Perdicas, after his father Alexander's death, had become passionately enamored with his father's concubine, Phila; who when the matter was communicated to her by Hippocrates, so accommodated her behavior toward the King that his health was in a short time completely restored." The later history of this accommodating lady we know not.

Various scattered anecdotes of Hippocrates and other people are told, and he himself writes of many places. Shortly after prescribing for Perdicas he was urged to go to Abdera, on the southern coast of Thrace, to combat the plague. That distemper was then ravaging the northern shores of the Ægean Sea, and distant peoples were clamoring for Hippocrates. It was the Plague of Athens, described centuries later by a brilliant young American.[†] The scourge lasted many years, moving slowly up and down the coast, and Hippocrates fought it here and there. Pericles died of it in 429 B. C., when it raged at Athens, and that year or in later years Hippocrates did what little he could for his beloved Athenians. In such scenes and so occupied he passed his long and active life. Artaxerxes in distant Persia heard wonderful tales of the famous Greek, and sent him a great fee to come to his court; but Hippocrates refused to listen. He was growing old then, the devastating Peloponnesian wars were wrecking his Greece, and he seems to have felt that his place was among his own people.

Hippocrates was a contemporary of Socrates, but he was a better practical philosopher. During his life men heaped honors upon him, and after his death they deified him. Even among his own Coans nothing was held too good for him. Indeed, he had helped those brethren of his in many ways which they could appreciate, and they marked him by an initiation in the sacred Eleusinian rites after a manner which no mortal since Hercules had enjoyed. A public entertainment was instituted in honor of him and his posterity.

In his old age, the length of which is disputed, Hippocrates went back to his favorite Thessaly. There he lived until nearly a hundred,—some say he was 109 years old,[‡]—and there he died in that Larissa whence he had gone to the rescue of love-sick Perdicas more than half a century before.

The Father of Medicine taught the "humoral theory" of disease; that the body contains four humors—blood, phlegm, yellow bile, and black bile, a right proportion or mixing of which constitutes health; improper

[*] John Moffat, M.D.: "Life of Hippocrates," London, 1788.

[†] E. H. Smith, in "New York Medical Repository," 1795.

[‡] The commonly given dates of Hippocrates are, 460 to 361 B. C.; but there is no certainty.

proportion or irregular distribution constitutes disease. That is a concise statement of the humoral theory, interesting to surgeons even. Most moderns, when they hear of Hippocrates, recall vaguely the humoral theory and the "Hippocratic oath."*

It is needless here to discuss at large his teachings. The "oath" indicates the dignity and honorable aims of the profession for him. Moreover, he was the first clearly to show that the study of disease must be through observation and deduction. With such tools as he could command he made his diagnoses and his prognoses. He and his disciples carried the art of prognosis far. Their conclusions were drawn from symptoms, but their rare patience in studying and recording these gave great value to their forecasts. In a word, that was scientific medicine.

One might devote a chapter to the surgery of Hippocrates.† He discoursed wisely and elaborately of fractures, of joints, of the structure and diseases of bones, of ulcers, of fistulas, and of hemorrhoids. A great deal that he wrote is sound still, though many of his conclusions do not coincide with those of modern experience; however, it is all much more final today than are his purely medical writings. The stamp of truth is on all the genuine Hippocratic work. He reported cases good and bad, and extenuated nothing in the telling. He dwelt also upon the patient's general condition as affected by special lesions; upon fever, delirium, wasting, and the constitutional tendency. He noted especially the breathing, the facial expression, pallor, the body temperature, and the appearance of the urine, feces, and blood. In addition to these elaborate dissertations, his writings deal with trephinings, with the reduction of hernia, with herniotomy, and with lithotomy by both the perineal and the suprapubic routes. He described pneumothorax and opened and drained the chest for empyema and hydrothorax. All these things and many others he did, and he seems to have done them well. The most interesting feature of his work for us is that he had a clear conception of a great number of surgical lesions, that he described faithfully and graphically what he saw, that he employed rational surgical methods of treatment, and that he taught others what he knew.

---

* This famous fragment of old days is still vibrant as many an ancient liturgy: "I swear by Apollo the physician, and Æsculapius, and Health, and Panacea, and all the gods and goddesses, that, according to my ability and judgment, I will keep this Oath and this stipulation—to reckon him who taught me this Art equally dear to me as my parents, to share my substance with him, and relieve his necessities if required; to look upon his offspring on the same footing as my own brothers, and to teach them this Art, if they shall wish to learn it, without fee or stipulation; and that by precept, lecture, and every other mode of instruction, I will impart a knowledge of the Art to my own sons, and those of my teachers, and to disciples bound by a stipulation and oath according to the law of medicine, but to none others. I will follow that system of regimen which, according to my ability and judgment, I consider for the benefit of my patients, and abstain from whatever is deleterious and mischievous. I will give no deadly medicine to anyone if asked, nor suggest any such counsel; and in like manner I will not give to a woman a pessary to produce abortion. With purity and with holiness I will pass my life and practice my Art. I will not cut patients laboring under the stone, but will leave this to be done by men who are practitioners of this work. Into whatever houses I enter, I will go into them for the benefit of the sick, and will abstain from every voluntary act of mischief and corruption; and further, from the seduction of females or males, of freemen and slaves. Whatever in connexion with it, I see or hear, in the life of men, which ought not to be spoken of abroad, I will not divulge, as reckoning that all such should be kept secret. While I continue to keep this Oath unviolated, may it be granted to me to enjoy life and the practice of the Art, respected by all men, in all times! But should I trespass and violate this Oath, may the reverse be my lot!"

† In Francis Adams's two-volume edition of the "Genuine Works of Hippocrates" nearly all of the second volume deals with surgery.

All this sound work so appealed to men in that ancient world of limited knowledge, that they came to regard the steward of a few things as the master of many things. Whatever Hippocrates taught was true in their eyes, and in the changes of idealistic philosophy which followed his era, men continued to cling to those facts which Hippocrates had given them.

GALEN.

131 TO 201 A. D.

Nearly five hundred years elapsed between the death of Hippocrates and the birth of Galen—half a millenium; a period equal to that which separates us from the battle of Agincourt and the ancient French surgeon, Guy de Chauliac. Galen revered Hippocrates and followed his teachings and quoted him in his books. Who quotes de Chauliac?

During those five hundred years after Hippocrates the world of politics had moved on, and the map-makers had been at their work. The glory of the Greece of Pericles had departed; Alexander had conquered his world and wept and died; under his lieutenants and successors a Greek Egypt had risen and decayed; Carthage had fallen; the Roman Republic had embraced the world and given place to the Roman Empire; Jerusalem had been destroyed, and Christianity was gathering strength for that sweep of progress which was to increase in proportion as Rome declined.

Surgical science could show no stupendous changes. Plato and Aristotle followed Hippocrates; Plato, the immortal idealist, but without the scientific method, influenced enormously the ancient world of thought; while Aristotle, with a keener appreciation of nature, taught surgeons the value of anatomy and some understanding of the inductive method.

After Hippocrates, our landmark is the Alexandrian School, important more especially because Galen studied there in its declining years. Galen was a Greek. You will observe that most of the famous physicians of the old Roman world were Greeks; the Roman genius failed to appreciate and cultivate medicine. As for Alexandria, its influence on the science of antiquity was enormous. Many teachers and schools arose there, and for nearly a thousand years it was the Mecca of medicine. Herophilus,* the great anatomist, taught there. Do we not recall him still in the torcular Herophili?† He founded a school, as did his rival Erasistratus. These men and their followers made famous that Greek city in Egypt, where most of the old-world surgeons studied and about which many of them wrote; Celsus, among others, at the beginning of our era, a scholar and compiler, rather than a practitioner, but often quoted as among the fathers. The one great thing accomplished by the Alexandrians was the study and development of anatomy by dissections. Let us remember them for that one thing if for nothing else, for from the decline of Alexandria to the time of Vesalius—nearly one thousand years—knowledge of anatomy made no advance.

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* A Greek of Chalcedon, born about 300 B. C.

† *Torcular*, "wine press."

Galen was a product of Alexandria. His is a notable name, and the man was a great man. Certain dyspeptic moderns have felt called upon to sneer at him because he knew less than we know; but let us remember that the second century was not the twentieth century, and that according to his lights Galen did a very great work. None but a great man could have controlled medical thought for nearly sixteen hundred years. He was a surgeon as well as a physician and a philosopher.

Claudius Galen was born in the year 131 A. D. He was an Asiatic Greek and his native town was Pergamus on the Caicus River, in southern Mysia. So he was almost a fellow-countryman of Hippocrates, for Pergamus was on the mainland, 155 miles due north of Cos. Galen was a handsome, vigorous, precocious boy, the son of a high-bred, cultivated, and wealthy father, Nicon, a professional architect, who devoted himself to the education of his promising son. The son passed his life among conspicuous scenes and notable men. He was extraordinarily able, steeped in Greek culture, and intolerant of humbugs and fools; not a comfortable man to live with, if one may judge from his own writings, for he was conceited and short-tempered,—a very different person from the steady, kindly, great-hearted Hippocrates; but his lines were laid in difficult times, and he scorned his superficial, cynical, flabby-minded professional colleagues of Rome, where his most productive years were spent. The history of Galen and his times is intensely interesting. To the twentieth-century reader none of the ancient physicians seems so modern, so vital, so human. His accomplished father destined him for a scientific career and had him carefully educated. He studied in the best schools; he was a pupil of the Stoics, the Academies, the Peripatetics, the Epicureans —and he was a faithful pupil. Though not robust in youth, he was active and well trained; his mind was acute, his memory retentive, his understanding just. Men would call him a genius, had not he succeeded the great master Hippocrates. Among his preceptors Galen mentions eight men—names merely, rescued from oblivion. Writers tell us that he was an accomplished physician at the age of eighteen, and that at twenty-one he had composed some medical works. In these days we accept with caution those tales of precocity. However, such learning and such giving forth seem to have been of the schools and not of experience, for Galen appreciated then, as he appreciated through life, that contact with the patient and with the organs of the body is essential. Then as now, too, the actual difference in knowledge of highly trained men was negligible. Distinction consists in exploiting knowledge and making it available.

At the age of twenty-one Galen lost his father. Then the wandering spirit seized him and he began his travels. The experience was such as our best cultivated men know today. He went for a time to Smyrna and Corinth for the lectures; then to Alexandria. He had an enormous ambition and a boundless curiosity. He devoured and digested all sorts of information. He worked hard for years over anatomy and physiology; he followed eagerly branches of pure science; he became accomplished in letters and the arts. After a year or more in Alexandria he pushed on, observing, comparing, noting,—through Cilicia, Palestine, Italy, Thrace, Macedon, Crete, Cyprus. He visited Lemnos; he traveled in Syria. Like a proper peripatetic, he went on foot, seeing things and remembering them afterward. Finally, in his twenty-eighth year, he went home to Pergamus and settled down to teach, write, and practise. After four years of such provincial life the magnetism of the capital of the world became too strong for him. Making an excuse of sundry civil disturbances and tumults in Pergamus, he set forth again and went to establish himself in Rome.

From his first going to Rome, through the rest of his life, Galen found little peace. He was a strong, outspoken character, always uncompromising, and he made enemies. The profession in Rome was debased. Science had almost ceased to exist there. Commercialism and quackery ruled; the Oath of Hippocrates was a dead letter. A careful writer recently has described the "Medicine and Doctors" of Juvenal.* Now, Juvenal belonged to the generation of Galen's grandfather, but the times had changed little, and for the worse. We must believe the great satirist, beside whose pictures those of Tolstoy pale, when he says that Rome was a vast den of thieves, that life there was intolerable, that decency was almost unknown, that the decalogue was shattered daily in every household; that the doctors were a parcel of vampires, mean-spirited, dishonored, ignorant,—preying upon their patients as upon each other; poisoners, procurers, extortioners. Indeed, that Rome was a sorry place for an honest man of science.

Galen sems to have thought at first that he could bring some decency out of the mire, some return to the spirit of science, but he came bitterly to comprehend the futility of such a hope. The men on the ground had the ear of the degenerate public, and, except among the more intelligent and the powerful as well as among the virtuous few, he found little favor. Fortunately for him, the intelligent and the powerful were more numerous than were the virtuous few, so that he secured work and eminent patrons. Among such distinguished persons he names Eudemus, a peripatetic philosopher; Sergius, prætor at Rome; Barbarus, uncle to the Emperor Lucius Verus, and Severus, the consul, afterward Emperor.

Galen lived and practised in the midst of such people for five years; then in disgust he went home for a short time to Pergamus, but was soon recalled to Italy by the Emperor, to attend him and to combat the plague. He was then about thirty-five years old, and from that time until the end of his life he worked on in degenerate Italy—a scientist striving not to be a courtier. It is not clear what sort of success he made of these strivings. Marcus Aurelius wanted to take him as his personal surgeon to the war in Germany, but Galen escaped that service and remained with the court in Rome. There are sundry tales of his cures—tales told mostly by himself, but he has something to say of his failures also. An American writer* dismisses him casually with the statement, "Perhaps the worst to be said of him is that he assisted in preserving the health of Commodus (son of the Emperor), and the best, that he maintained much the same position in medicine as that occupied by Marcus Aurelius in philosophy." Fanciful as is such a comparison, it is certain that both men impressed themselves upon human thought for centuries: Galen growing dim in recent times—an authority no longer; Marcus Aurelius, the emperor philosopher, looming larger through the years.

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* Eugene F. Cordell, M.D., in "Medical Library and Historical Journal," vol. 8.

So far as Galen's life is known to us, however, and long as that life was, there is little more to say of it. He went on with his working and writing; he continued to cultivate the hatred of his colleagues, and he enjoyed to the end the confidence of powerful friends. The exact date and place of his death are not clear. Probably he died in Rome in the year 201 A. D., when he was nearly seventy years of age. However, the surgical achievements of the man must engage us now, and some attempt to explain what it was he did, and why it is that he remains the second great medical prophet of antiquity.

The fundamental reason for Galen's great and sustained reputation is his constant employment of demonstration and his reliance on rational and intelligible evidence. In a broad sense he was a faithful disciple of Hippocrates, for he followed the great master in practising and teaching the essential importance of the study of vital phenomena. Hippocrates confined himself to bedside investigation. Galen went further; he practised and taught laboratory methods through animal experimentation. He was truly our first great physiologist. Mark some of his writings and their bearing upon surgery as a therapeutic agent, remembering at the same time that surgery and medicine had not then suffered that artificial divorce which so crippled scientific progress in the middle ages, and to no small extent does still cripple it. Galen appreciated, as did those other ancients, that physiology is physiology, that diagnosis is diagnosis, and therapeutics, therapeutics, with surgery a branch of therapeutics.

Perhaps his most famous discovery, and the one for which he is best known, is that of the true function of the arteries. Previously, arteries had been held to contain air, as their name implies. He recognized that arteries in the dead appear to be empty or to contain air, but he demonstrated by the double ligature of an artery on a living animal, and subsequent section of the vessel between the ligatures, that the artery is distended with blood. He observed, too, that arterial blood differs from venous blood, and this phenomenon he ascribed to the entrance of some vital element of the atmosphere through the lungs into the arterial system.

More remarkable still, he asserted a fact which even Harvey fifteen centuries later did not observe—that there is a terminal communication between the two sets of vessels, veins and arteries; and he used our present word *anastomosis:* "The arteries and veins anastomose with each other throughout the whole body, and exchange with each other blood and spirits by certain invisible and exceedingly minute passages."[*]

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* David Hunt: "Boston Med. and Surg. Journal," vol. cxxxi, 1898.

Galen studied the heart also and described its movements in a fashion not unworthy of Harvey. He wrote: "We can also see the arrangement and action of the fibers of the heart under two conditions, either by examining the organ when just taken out of the animal and still pulsating, or by removing the sternum in the manner which I have described."[†] And let anatomists note that fourteen hundred years before Botali he described the foramen ovale and the ductus arteriosus. He described them as physiologically associated, and as belonging to the fetal condition.

Of supreme interest to surgeons is the fact that Galen knew and practised the ligature of arteries; though it does not appear that he applied the principles to vessels severed in amputations—a principle the establishment of which immortalized our sixteenth-century Paré. In his treatise on tumors Galen describes aneurisms, true and false, and recommends compression for their cure. He preceded Antyllus, whose famous operation for aneurism is still taught in our schools. Antyllus wrote toward the end of the third century, and our knowledge of him comes to us through the encyclopædic Oribasius, physician to the Emperor Julian (361 to 363). Certain it is, therefore, that the daring operation of double ligature and incision was unknown to many-sided Galen.

The nervous system was Galen's favorite field of investigation. He regarded the brain as the central organ from which the spinal cord is an offshoot, and recognized that the nerves are structures designed to convey impressions of sensation and motion. He taught that "the muscle is the instrument of voluntary motion; and we have seen whence the principle of this motion originates, and by what path it travels. It comes *from* the brain and *through* the nerves."

The functions of the cord, too, received his elaborate consideration, and to all of his statements he brought experimentation for proof.[‡]

He advocated, accordingly, sundry operations for injuries to the brain and cord, and he advocated them intelligently. Others among the ancients were familiar with such procedures, but much of Galen's writing has a curiously modern sound. He used the trephine on the head less than did others of his time, for he preferred the gouge and chisel. In injuries to the spine with compression of the cord he appreciated the condition, made a proper diagnosis, and advised an operation for relief.

Briefly recorded, such are some of the achievements of this remarkable man. Doubtless many of his views were erroneous and his advice unsound. He was a voluminous writer, who felt that his mission was to instruct the profession in every branch of medicine. Often he was visionary; often, for lack of the microscope and of a knowledge of chemistry, his assertions were mere guesswork and his hypotheses untenable; but, with such light as he had, his methods and purposes were correct. If he had lived in more settled times and among a people sensible of the meaning of science as he taught it, there can be no doubt that the impetus he gave to medicine would have broadened into great schools of learning such as the world had to wait for during nearly eighteen centuries. With his death and the passing of his immediate successors progress languished and expired, for the ancient world was dying and was bearing down with it the humaner arts.

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[*] "De Usu Partium," vii, 10.

[†] Ibid., vi, 8.

[‡] Vide "De Hippocratis et Platonis Placitis," vii, 8; "De Administrationibus Anatomicis," vii, 9, 10; "De Locis Affectis," iii, 14.

The significance of all this belongs to the domain of world-history rather than to this simple narrative; but the course of world-history bears immediately upon our theme. That corrupt, besotted, old civilization must needs have been destroyed. The rough, wild, clean-bodied barbarians had to be turned loose for centuries over the earth to sweep it clean, else had mankind expired of very rottenness. For generations it seemed that the Church alone had survived—that wonderful Church, adored, feared, reviled, misjudged, and misjudging. Now a sink of superstition and cruelty and folly; again the staunch, unterrified, unbroken guardian of shattered civilization; cherishing, ignorantly often, but jealously and fiercely, the records of a past science. It is the fashion of writers bitterly to accuse the Church of standing doggedly across the path of knowledge and persecuting the disciples of truth; and doubtless the charge is a thousand times just, but we must remember also that what little western learning survived through the dark ages was stored and guarded in monastic vaults and clerical libraries—wealth unrevealed and unknown even to the custodians, but still in some fashion preserved for the enlightenment of wiser generations.

Briefly, then, what have we seen to be the course of medical science? Among the Greeks medicine held a high place, for the Greek genius was most conspicuous in the affairs of civil life and the realm of intellect. Among the Romans, military affairs were regarded as most worthy the attention, and this worship of physical force stunted eventually intellectual growth and pursuits. After the republic, the rise of a military aristocracy accentuated still more this tendency, and made permanent the inferior position of the learned professions, especially of medicine. During nearly two thousand years this Roman influence maintained, for even after the rise to power of the Church of Rome the soldier continued to be regarded as the superior of the priest. First the soldier; second the priest; third the lawyer; fourth the merchant; fifth the physician, and then after a long interval the surgeon, ranking with the humblest of craftsmen.

VESALIUS.

1514 TO 1563.

Andreas Vesalius was born on the last day of December, 1514—nearly thirteen hundred and fourteen years after the death of Galen. Imagination is staggered by the attempt to grasp in detail that mighty span of centuries; yet the meanest imagination among us could measure with a foot-rule the intervening progress in science. Galen's works were textbooks still. Names are named in the interval, and a few good surgical writers,—Antyllus and Oribasius already noted, Ætius Amidenus, Alexander of Tralles, Paul of Ægina,—all belonging to the old order. Then there were the Arabians, Avicenna (980–1037 A. D.) and Albucasis (died about 1105 A. D.).

Those Arabians are worth noting as we pass. Medical science must generally be looked for at its best among forward and active peoples, and during the middle ages the Arabs were conspicuous in the world's history. Both Avicenna and Albucasis were authorities for centuries,—not so much for any new thing they did as for their compiling and bringing before the medical public, such as it was, the best ancient teaching, otherwise lost or forgotten. In a way they were necessary to Vesalius.

Vesalius is a landmark in our course because he did new and important things. He cast aside tradition and saw with his own eyes. Men say that he overthrew Galen; but in truth he was the follower of Galen in science—the first man known to me, for thirteen centuries, to adopt and practise the methods of that ancient master. He improved on Galen, he corrected many of Galen's errors, he came to be a man full of novel lore; but why disparage Galen? Do not we twentieth-century students know things undreamed of by Hunter, Rush, or Drake? Vesalius is not generally reckoned among the surgeons; indeed, surgical writers pass him by and tell rather of his contemporary, Ambroise Paré, of whom we shall hear; but today Vesalius would properly be regarded as a surgeon. He held a chair of surgery; he was a profound student, the founder of modern anatomic research, the man who made possible for us a development of surgical science.

Fain would one dwell upon those wonderful years of the sixteenth century, when Vesalius lived and taught. We are wont to sum it all up in the word Renaissance. That was the springtime of our world. Great names crowd the text—Luther, Michælangelo, Raphael, Titian, Copernicus, Columbus, to go no farther. Men were breaking away from tradition, the dark veil of the middle ages had been rent. In the midst of such stirrings Constantinople fell before the militant Turk, and wise men fled from the ancient capital, bearing with them, for their western brethren, forgotten treasures of Greek literature and science.

The story of Vesalius's life is far different from that of the rude craftsmen who composed the surgical guild of his day. He was a cultivated product of the great universities, with learning as well as genius, and he came to appreciate early the importance of anatomy and its bearing upon surgery.* He was born in Brussels of an excellent burgher family, established for generations at Nymwegen. His traditions were of the best, for he came from a line of physicians and learned men. His father was apothecary to Charles V. Like Hippocrates and Galen, Vesalius was carefully educated, and spent many of his youthful years at the famous old University of Louvain, not far from home. Alas, for our lack of space! that old university life is a subject worthy of study.

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* "Vesalius: His Forerunners and Followers," Lecture I, in "The History of Physiology," by Sir Michael Foster, 1901.

The lad was born with a passion for dissecting. At Louvain he had to be satisfied with animals. Then, at eighteen, in 1533, he went to Paris to learn of Sylvius (Du Bois)—that Jacobus Sylvius after whom the fissure is named.

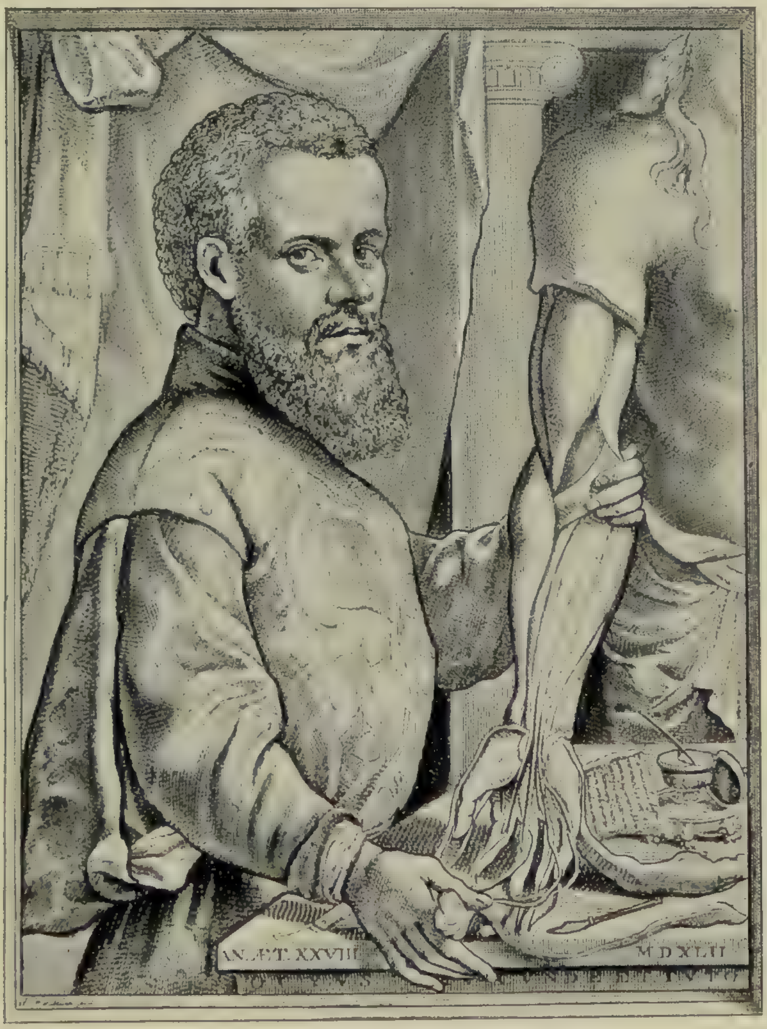

FIG. 1.—ANDREAS VESALIUS.

Sylvius was no surgeon, he was not even a great anatomist. He was a lecturer who read out of Galen to his pupils sitting about, with an occasional dead body before them. Now and then, by direction of the master, the crude barber assistants exposed roughly some structures for the gaze of the audience.

This was futile work. Stories are told of Vesalius's impatience; one of them that at the third demonstration, exasperated by the ignorance displayed, he thrust aside the stupid assistants and showed with his own hand how the dissection should be done. That anecdote is the key to the man's life. Anatomic research, applied anatomy, physiologic deductions from such tasks, surgery, and general practice were to be his work, but always he turned back with almost fierce joy to anatomy and surgery. He spent three years of study in Paris; then another year in Louvain, where he issued his first publication,—a translation of the ninth book of the Persian, Rhazes,—and then he went to Italy, where his masterpiece was to be accomplished. It is interesting to note that while a lad in Venice he probably knew the young monk Ignatius Loyola, founder of the Order of Jesus.

The abilities of Vesalius must have been brilliant and conspicuous, for almost at once he attracted the attention of leading men in Venice. He was granted the M. D. of Padua in the same year, 1537, and soon afterward, when but twenty-two years old, was given the chair of Surgery and Anatomy in that University.

Opportunity for anatomic study was greater then in Padua than anywhere else in Europe. The authorities were nursing the University and the restraining hands of the Church were held off. For five years Vesalius worked there with enormous success. He was instantly popular as a teacher; he was an inspiration to thousands of students. He told them what he knew, and, most important of all, he taught them the scientific method. He killed and buried the old system of authority in anatomy. Though the edifice of speculative medicine survived for many years, he weakened its foundations.

In 1543, the sixth year of Vesalius's life at Padua, he published the "Fabrica Humani Corporis." Promptly the heavens were opened, and the wrath of entrenched conservatism descended upon him. Just before his book appeared he had left Padua for a time, with the consent of the Senate, and it was during this absence that the storm raged. His old master Sylvius and others thundered against him for daring to point out that Galen was wrong. He returned to Padua after a year, but found that even there opposition to him was strong. He gave a few lectures in Padua, Bologna, and Pisa, demonstrating again on the cadaver the truth of those things he had published, but at last, wearied of persecution and contemptuous of his weak-kneed world, he gave up his career and accepted the post of court physician to Charles V.

There is little more to tell. Vesalius continued in the service of his patron. Twelve years later, on the abdication of the Emperor, he was transferred to Philip II. He chafed against the life; now and again he attempted to break away. Then in 1563 he started out on a pilgrimage to Jerusalem. He visited Venice. He renewed former friendships. We can believe that he may have intended on his return from the East to continue the pursuit of science as of old; but fate overtook him. He did not live to see his Padua again; he was taken ill on the voyage home, was landed on the island of Zante, and there died in his fiftieth year.

AMBROISE PARÉ.

1510 TO 1590.

We hear a deal of talk about "barber-surgeons" and "surgeons of the long robe"—to our confusion often. Ambroise Paré was a surgeon of both sorts. Let us get clearly in mind the distinction; learn something about the status of surgery in those centuries, and then hear something of the life of that famous man.

We know how in Paré's time the Church had controlled all European learning for years, save for what the Arabians taught to a few daring and ambitious travelers. In the days of the fathers and in the middle ages, healing was one of the priest's functions. But the shedding of blood was abhorrent to holy men, so they dealt with internal medicine only—in feeble and superstitious fashion, though they had some skill in the treatment of wounds. In such tasks good women, too, had their share; but surgery—the actual shedding of blood—was left to the Jews and to the profane and vulgar. Now, in the dark ages it came about that tonsures

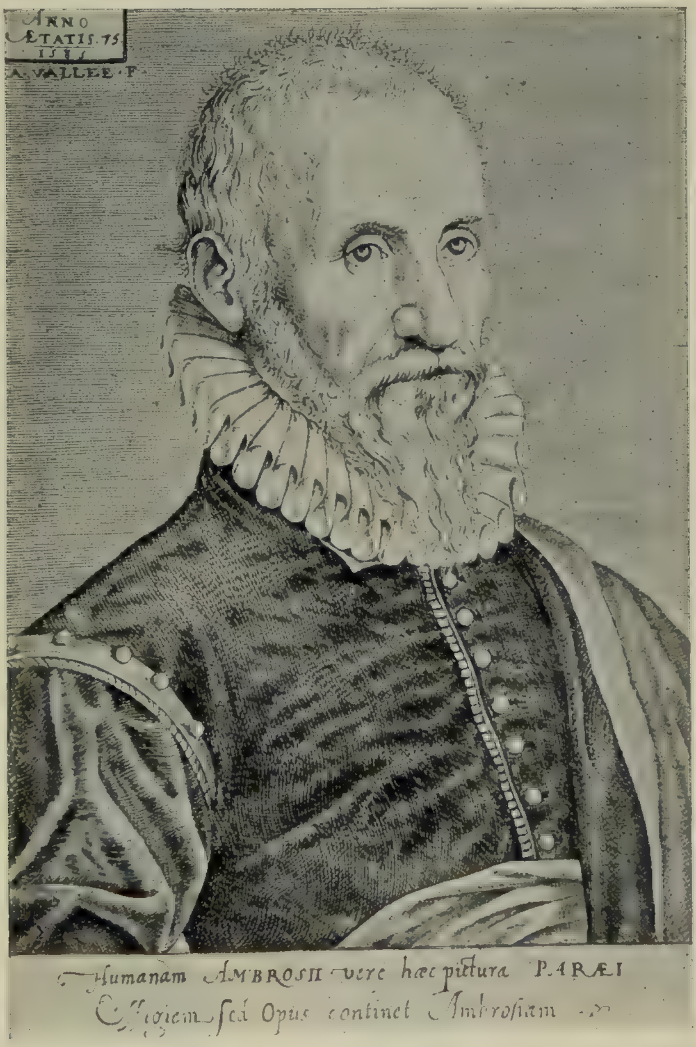
ANNO
ÆTATIS 75
1585
A. VALLEE F
Humanam AMBROSII vere hæc pictura PARÆI
Effigiem ſed Opus continet Ambroſiam

FIG. 2.—AMBROISE PARÉ.

necessitated the presence of barbers in the monastaries; besides the tonsure, regular bleedings were prescribed for certain orders. The much-quoted Gardner* tells us that both duties—shaving the heads and bleeding—fell naturally to the same officer, and there we see the origin of barber-surgeons.

This combination of functions flourished in France. The common barber there was a despicable creature, and the barber-surgeon, too, was contemptible. In Italy, with its greater enlightenment and higher standards of education, the same odium did not attach to the barber-surgeon's office. French customs ruled in northern Europe, however, and the surgeons of England and Germany ranked with their Gallic brethren. So let us observe the situation as it developed in Paré's France.

Long before his time there had grown up a class of regular *physicians*—men educated in a fashion, compelled to know and speak Latin, licensed to practise. They were the great men of the profession, the men at the top, as the barber-surgeons were the men at the bottom. Between the top and the bottom was a third body of practitioners, surgeons proper, who came to be known in France as the confraternity of Saint Cosmo or St. Côme. These were the "surgeons of the long robe," while the barber-surgeons were "surgeons of the short robe." The three sets of men—physicians, surgeons, barber-surgeons—were for long in conflict, as was inevitable. The short robes poached on the preserves of the long robes; that is to say, they went out of their sphere as bleeders and minor operators, and undertook serious major operations. The long robes, who were better educated men, presumably learned in the great writers, and speaking Latin, attempted constantly, by prescription and legal means, to put down these upstarts. At the same time the long robes offended the physicians by prescribing drugs and undertaking general practice. So the long robes were at feud with the men above them and with the men below them.

We need not follow in detail their endless wrangles. Until modern times the physicians maintained their position of superior equipment and authority, but there was constantly a gradual leveling up of the two inferior orders, until in the eighteenth century a broader and more scientific basis for surgery was established. Finally in Paris the confraternity of Saint Cosmo gave way to the Academy of Surgery in 1731, with the great Petit as director, and still later there was added to this the École Pratique de Chirurgie, with Chopart and Desault among its professors.

Ambroise Paré began life as a humble barber-surgeon, and ended as the greatest surgical authority in Europe, and the best beloved man in France. He was not trained in the schools; he was not a great scientist, as was Vesalius. He was a practical clinician, who went through the world with his eyes open, and brought to bear upon his task hard common sense, impatience of vapid tradition, and an enormous experience.

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* John Gardner: "Sketch of the Early History of the Medical Profession in Edinburgh." Edin., 1864.

Paré was born in 1510 in the village of Bourg-Hersent, now part of Laval, in Maine. His father was a servant, possibly a valet and barber; his brother Jehan and his brother-in-law, Gaspard Martin, were barber-surgeons. We have a great deal of light on the training and career of Paré. The student of those times may read the volumes of Malgaigne or the "Life" by Paget. Paré was apprenticed early to a barber-surgeon, and then, in 1533, at the age of twenty-three, he went to Paris, where the plague was raging and work was to be done. Louis XII had died in 1515, and Francis I was king. Paré was destined to see Henry II, Francis II, Charles IX, Henry III, and Henry IV.

Almost at once the young surgeon was appointed a resident in the Hôtel Dieu, that famous hospital then already nine hundred years old, and there he served as pupil, dresser, and operator for three years. Vesalius, who was four years Paré's junior, had just left the place, but they served the same masters and heard the same lectures, for Sylvius taught them both. They were to meet at last after many years—for there is reason to believe they consulted over the death-bed of Henry II in 1559.

Paré's three years of service in the hospital laid the foundation for his remarkable and romantic career.* On leaving the Hôtel Dieu in 1537 he does not appear to have taken with him any special license save his acknowledged ability and a sanguine enthusiasm. He craved more experience and he looked for a permanent abiding-place. So he went to the war in Piedmont, but first made an establishment in Paris. In that way, as Paget says, the two streams of his life flowed on side by side for many years. He was with the army in time of war, he practised in Paris during the intervals of peace.

When Paré was old there was a man living in Paris to whom we owe a great deal. He was one Etienne Gourmelen, Dean of the Faculty of Medicine, and he was a wrong-headed person. In 1580 he published a book, and in his book he attacked Paré. This drew from Paré his famous "Journeys in Diverse Places" (1537–1569), without which our surgical literature would be the poorer. The "Journeys" tells the surgical history of Paré's life, and the wretched Gourmelen is flayed incidentally.

You must take for granted the charm of Paré's tale. A brief outline of it is this, that in 1537 he went off to the wars as an independent surgeon with one Colonel Montejan. In those days there was no organized army medical service. Paré picked up his work and experiences where and as he could. He attached himself to one great man or another for many years, until in 1552 the king appointed him one of his surgeons-in-ordinary. In 1541, when thirty-one years old, he had qualified as a master barber-surgeon.

There was no regular salary for such services as Paré gave, but fees were manifold and often eccentric. We read that at one time he received a cask of wine, at other times fifty double ducats and a horse, a diamond, a collection of crowns and half-crowns from the ranks, other "honorable presents and of great value"; from the king himself, three hundred crowns; another diamond, this time from the finger of a duchess; and a soldier once offered to him a bag of gold.

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* For a delightful account of "Ambroise Paré and His Times" I refer the reader to Stephen Paget's book. G. P. Putnam's Sons, 1899.

Men showered gifts upon him and the army always loved him. His presence alone came to be regarded as equivalent to ten thousand reinforcements. He was the intimate friend of generals and the idol of their troops. He was sane, humane, resourceful; abounding in common sense, in shrewdness, in natural ability. He weighed and winnowed authority; he dared to have original opinions. He loved the people, but he did not hate their rulers; he was loyal, quiet, conservative; Paget says that "he was a man who heartily disliked change, self-will, scepticism, controversy, politics and foreigners." Paré's personality counted greatly. It was so with him as with Boerhaave, and Charles Lamb, and other great ones we know; but he did things, too, for which we must remember him. He made important discoveries and he wrote about them. His publications number eleven and treat of an enormous variety of subjects, professional and extra-professional.

Paré dealt rationally with gunshot wounds, showing that they are not necessarily poisoned and that cleanliness and support often suffice for their cure. He wrote elaborate treatises on anatomy and surgery; a special monograph on head-injuries, and on the plague, smallpox, measles, and leprosy. These were some of his strictly professional writings, and then there was that account of army adventures and military surgery in his "Journeys." He was an eager and vigorous writer, with the story-teller's instinct and a sure sense of proportion. He makes his points firmly and boldly, leaving one ready to hear more. He was as original in his writing as in his practice. He was the first of our great modern clinical surgeons, just as Vesalius was the first of our modern scientists. He made careful and exhaustive diagnoses, he spared the knife so far as possible, he was dextrous and nimble but never slovenly. He was especially skilled in the dressing of wounds, and prided himself on making his patients comfortable. His bandaging was a work of art, for he insisted that the rollers should be neatly and accurately made, and he applied them himself smoothly and deftly.

Paré is known to most of us for two great improvements in our art—a simple treatment for wounds and the use of the ligature in amputations. Space does not permit me to elaborate these two matters; suffice it that he came upon a let-alone treatment of wounds, at Turin, in his first campaign. Old custom prescribed that wounds, and gunshot wounds especially, should be treated with boiling oil—an agony to the patient and the cause of delayed healing. At first Paré used this method fearfully, but after one severe engagement his oil gave out, and he had to content himself with an extemporized simple ointment. To his surprise and joy he found the next day that his patients thus treated had fared better than the others. Former men had seen the same thing, but he had the genius to take to heart what he saw, and ever afterward, against bitter opposition, he taught the humane treatment.

Paré's use of the ligature for arteries instead of the old cautery came about in a somewhat similar fashion. In 1552 he was with the army besieging Danvilliers: "There was a culverin-shot passed through the tent of M. de Rohan, which hit a gentleman's leg, which was of his household. I had to finish the cutting off of it, which I did without applying the hot irons." He used the ligature and was delighted with the result of his experiment. We know how Galen had ligatured vessels wounded in continuity, but it is to Paré that we owe the end ligature in amputation stumps. Such teaching was revolutionary; it brought upon him the wrath of conservatives, and to the outpouring of such wrath by the foolish Gourmelen we owe such tales as that of M. de Rohan's unfortunate gentleman.

Paré's life was adventurous and brilliantly useful to the last. He was always in the public eye; he saw constant service. In the field it is a story of battle, murder, and sudden death; in Paris it is a record of plague, pestilence, and famine. The end came in December, 1590, when he was eighty years old. He had escaped the St. Bartholomew massacre, he had lived through the wars of the Huguenots, and he died the year of the battle of Ivry, of the siege of Paris, and the final triumph of the house of Bourbon.

ALBRECHT VON HALLER.

1708 TO 1777.

Ambroise Paré wrote in his dedication to the king, of his edition of 1575: "God is my witness, and men are not ignorant of it, that I have labored more than forty years to throw light on the art of surgery and bring it to perfection. And in this labor I have striven so hard to attain my end, that the ancients have naught wherein to excel us, save the discovery of first principles; and posterity will not be able to surpass us (be it said without malice of offence) save by some additions, such as are easily made to things already discovered."

Now, this amazing statement proved fairly sound. In the *art* of surgery after Paré there was no great or radical progress for many generations; indeed, the art of Paré would not have been unworthy the art of Wiseman, of Petit, of Sabatier, of Hunter, or of Cooper even, for not until two hundred and fifty-six years after Paré's death was anesthesia made certain to a waiting world; anesthesia, to be followed by asepsis and the art of modern surgery.

But between Paré and Lister the *science* of surgery did not stand still, for the science of surgery is but one expression of the noble science of medicine.

During those vital centuries anatomy was revised, histology and chemistry were born, and physiology was reborn; the great science of pathology itself came to be intelligently studied; embryology was developed, and the uses of the microscope were made known, in a limited way, to laborers in all these fields. If this were a history of medical science as a whole, volumes might be written on what was doing during those centuries, but our task is to note merely some of the benefits which that developing science brought to surgery, and to name a few names. The work of Borelli, Malpighi, Paracelsus, Van Helmont, and Harvey concerns us. Borelli was a physicist and physiologist, who worked out the uses of the muscles. Malpighi, one of the greatest of physicians, demonstrated the anatomy of the liver, the kidney, the lungs, the nerves, and the skin. He saw the red blood-corpuscles and he discovered the capillary circulation. Paracelsus burned Galen, threw away traditional therapeutics, and pointed the road to modern chemistry. Van Helmont elaborated the crude teachings of Paracelsus, while the great Harvey, surgeon as well as physician, capped the work of the Continental investigators by his demonstration of the proper functions of the heart and of the circulation of the blood. In such breathless fashion we must brush past great names and events until we come to another milestone on our road—Haller, of Bern and Göttingen. He was a professor of surgery and a physiologist, a teacher rather than a practitioner, but surgeons properly may claim him as their own. As Foster says:* "When we turn from any of the preceding writers on physiology and open the pages of Haller's 'Elementa' we feel that we have passed into modern times."

Albrecht von Haller was born at Bern of a good Swiss family on October 16, 1708; and having done sundry notable things in various parts of the world, he died in Bern in 1777.

It was a marvelous mind, colossal, wide-grasping, omnivorous, retentive, belonging to a domain wider than surgery; but surgical problems occupied some portion of the man's life.

A word about his life: As a child he was sickly and precocious. He mastered strange tongues and was little regarded by his seniors. When less than ten years old he wrote a Chaldee grammar, a Greek and Hebrew vocabulary, Latin verses, and numerous biographies. While still a youth he wrote translations of Horace, Ovid, and Virgil, and an epic poem of 4000 lines on the origin of the Swiss Confederation. He was no prig, and people seem to have loved him even when they could not understand him. But he was little given to sports, and the young men, his comrades, saw in him a paragon rather than a playmate.

When thirteen years old Haller lost his father, and then for a time he went to Bienne, where he studied science and philosophy. After two years there he went to Tübingen for a year, and then at the age of seventeen to Leyden, where he began his formal medical studies. Albinus the younger was teaching anatomy there in that year of 1725, and Boerhaave was drawing from all parts of Europe and from America those great classes which have helped to render him immortal. Immortal he is in some fashion, and in spite of sneers. He was a tireless collector and an inspiring teacher, and in such teaching Haller found his opportunity.

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* "History of Physiology," page 207, by Sir Michael Foster.

At eighteen Haller finished with distinction the prescribed course of medical studies, and passed the following year as a graduate student in London, Paris, and Basle; of such wanderings and studies there is no time to speak, but they were fruitful even to the youth not yet twenty. The chroniclers tell next of his return to Bern to become a practising physician. There he worked for six years. He was not a success as a practitioner. The people of Bern were not used to that style of man and shrank from calling him in. But he studied. Ye gods, how he studied! He seems to have devoured the whole known range of medical authors. He read day and night—at his meals, at the bedside, on foot and on horseback, in his travels and at home. He read, and he remembered what he read. He investigated, too. He explored those wonderful mountains among which he was born, and he came to know his Switzerland as no other man has known it. Besides medicine, he devoted himself to botany, and produced a great work on the Alpine flora. He was a poet.

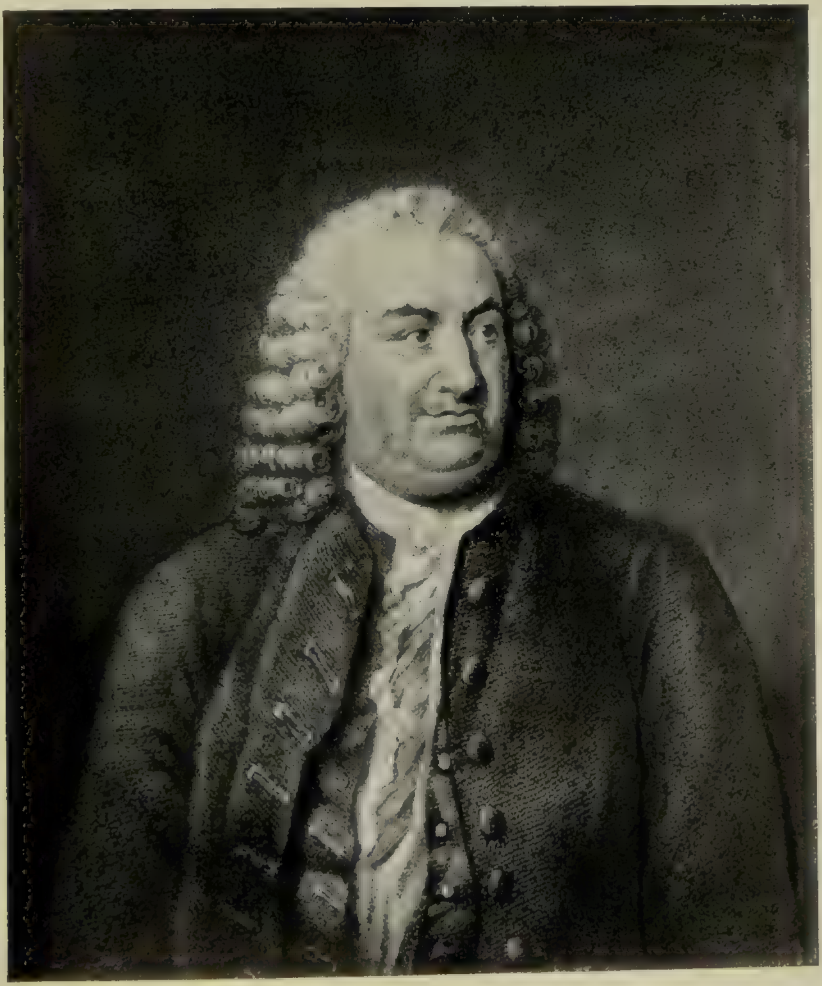

Fig. 3.—Albrecht Von Haller.

Still he was without honor in his beloved fatherland. But other people honored him. The scientific world was looking toward him, was reading his books on anatomy, physiology, and botany, and his poems too. In those years men were establishing a new University at Göttingen, in the domain of that sturdy George II who ruled England also; and casting about for professors in 1736 they called to them the young doctor of Bern. Haller went gladly, because he hungered for peace and for escape from Philistia. He went to Göttingen, to the chair of Medicine, Anatomy, Surgery, and Botany—to a mighty task. For seventeen years in Göttingen his labors were unceasing. He executed faithfully the enormous duties of his office, he stimulated students as none but Boerhaave had stimulated them for centuries. Against modern teachers of science the reproach has been made that they are professional teachers and amateur scientists. One could bring no such reproach against Haller. He knew most things that had been written of ancient science, and winnowed the chaff. But, more than almost any other man who has shared our labors, he possessed that rare type of mind which adds to knowledge. He told men what he had discovered. He excelled as student, investigator, teacher; and during those years the University became famous through all lands.

He went to Göttingen at twenty-eight and he left it at forty-five. Scientists deplored his leaving, and the great ones of the earth tried vainly to hold him back. He had been ennobled and courted by kings, and had sat in the seats of the mighty; but his was a homespun soul, quickly wearied by names and dignitaries. He threw over all, even the beloved society of scholars, and went back once more to his Switzerland. There he persisted in mighty works for twenty years—almost to the day of his death.

Of what sort, then, were those works? How does he touch us surgeons, and why do we claim him? Let a few halting words suffice as answer.

Most important of all, perhaps, he lectured on surgery for seventeen years. Two generations of students heard him. Fain would one have known that privilege. And he published two volumes, "Bibliotheca Chirurgica" (Bern, 1774–75)—a great work dealing with the literature and history of surgery. Its like is to be found nowhere else. So he grouped together the accomplishments of the past and made them available for modern men. Those volumes alone rank him among the most valuable contributors to surgical science, and that though he was no craftsman, and never operated, so far as we can learn. More important for us, however, than those great volumes was his teaching surgeons how to study, and his raising the profession from the degraded place in which popular opinion was holding it. In much of that he resembled and anticipated John Hunter. Haller grasped the wide significance of surgery and showed that it was far more than a mere craft. He brought to bear upon it a profound knowledge of anatomy, a keen-eyed devotion to physiology, and an enthusiasm for pathologic anatomy. He showed the absurdity of the medieval custom which had divorced surgery from medicine and a liberal education, depriving it of the services of distinguished men and cultivated minds. By his example he did more even than by his preaching; he became a great experimental physiologist; through such endeavors he made possible the practical investigation of natural processes, and through such investigations it has come about that numberless procedures of today are feasible and life-saving. His researches on the mechanics of respiration were striking and important; he studied and explained the formation of bone and he developed the science of embryology. Most important of all, perhaps, he established the doctrine of muscular irritability. Says Foster: "Conspicuous is the absence from his writings of loose expressions and ill-defined general views such as abound in so many of his predecessors. We may take any part of his great work as a trustworthy account of the knowledge of the time with regard to the questions therein treated."*

The problems of digestion also received his attention, and the modern surgeon who operates upon the bile-passages, the stomach, the pancreas, and the intestines may read with profit and pleasure what Haller has to say regarding the functions of those organs. He lived before the development of organic chemistry, but in treating of the pancreas he says: "A part, at least, of the usefulness of the pancreatic juice will be to dilute and soften the cystic juice * * * so that this mixes better with the food. Whence you may explain the hunger of the animals from which the pancreas has been removed, attributing it to the reflux of a slacker bile into the stomach"; and he ends: "There may be other functions of the liquid not as yet well known to us," prophetic of the work of Claude Bernard, a hundred years later.

We need not consider here Haller's elaborate work on the central nervous system, his almost modern conception of the functions of the brain and the purposes and uses of the nerves. Much of it was blind work, groping work if you choose, for he had to build up his hypotheses from experiments made with difficulty and often ineffectively, lacking our elaborate laboratories and our instruments of precision. We have indeed gone forward in a thousand ways, but we must look back to Haller as one of the greatest of the fathers, and admit that recent progress is due to the fact of our having worked upon his lines.

Such in broken outline is a sketch of Haller's great labors, and in such labors he continued nearly to the end of his life. In youth and early manhood at Göttingen he studied and taught and stored, giving forth here and there as special interests and occasion offered. In his maturity at Bern he produced his important writings, and the impulse of those writings is still upon us.

There was invalidism in his life. It was a mighty soul in a feeble body. He suffered much. In old age he was forced to the use of opium, and he died with finger on pulse; his last words, "The artery no longer beats."

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* Ibid., page 207.

JOHN HUNTER.

1728 TO 1793.

> "Up from Earth's Center through the Seventh Gate
> I rose, and on the Throne of Saturn sate,
> And many a Knot unravel'd by the Road;
> But not the Master knot of Human Fate."

In Scotland have appeared two men—Hunter and Lister;—great men in the history of surgery. Hunter dominates the eighteenth century, Lister is conspicuous in the nineteenth,—a man whose fame is destined to grow with the lapse of years. Hunter was greater than Haller in his influence on the practice of surgery, though the balancing of great men against each other is profitless. Hunter, Haller, Morgagni, are the famous names for us in the eighteenth century—Morgagni, pathologist; Haller, physiologist; Hunter, pathologist, physiologist, surgeon. It was time for Hunter. Since Vesalius and Paré, experience had been accumulating, research had been extended, books had been written, and knowledge had been diffused. Many able surgeons also had lived in this interval: Hildanus (1560 to 1624), the "Father of German surgery," a title properly belonging to Heister; John Schultes or "Scultetus" (1595 to 1645); Matthæus Gottfried Purmann (1649 to 1711?), a celebrated German; the Englishman, Richard Wiseman (1622 to 1676); known as the English Paré; Alexis Littré (1658 to 1726), who proposed inguinal colostomy in 1710; Jean Louis Petit (1674 to 1750), the great French teacher and reformer; Henri François le Dran (1685 to 1773), Claude Nicolas le Cat (1700 to 1786), the lithotomist of Rouen; Dominique Anel (1678 to 1725?), of aneurism fame; Jean Louis Belloq (1730 to 1807), who invented the nasal canula. Among the contemporaries and seniors of Hunter were Pierre Joseph Desault (1744 to 1795); François Chopart (1743 to 1795); Raphael Bienvenu Sabatier (1732 to 1811); William Cheselden (1688 to 1752); Percival Pott (1713 to 1788). Such are a few of the striking names in the surgical literature of the period. All of those men were able, active, and highly intelligent practitioners. Most of them were popular teachers and reformers; they devised new instruments and procedures, they perfected old measures, they adopted and utilized new discoveries, they raised the standard of education, and they abolished the barber-surgeon. But there was no prophet among them. Haller, indeed, was a marvelous investigator and teacher, but he was not a practical surgeon, and his discoveries came slowly to fruitage. John Hunter was the man for whom the profession waited.

Not long ago a well-known teacher, in addressing an audience of physicians, said: "Surgeons in the past have devoted themselves to the studies of anatomy, pathology, bacteriology, but they have neglected physiology. It is to the teachings of physiology that the surgeons of the future must turn for advancement in their art." He forgot John Hunter. An English writer has told us that to Hunter's sound teaching of anatomy, comparative anatomy, and pathology, and to the methods he employed and demonstrated to Jenner, Cline, Cooper, Abernethy, Home, Physick and a host of others, the great nineteenth-century school of English surgery owes its fame. All that is true, but Hunter did more than that. He was a great philosopher in the broad sense, as well as a student of the natural sciences. To this day his genius dominates and inspires our science. For nearly one hundred years the Hunterian Oration, instituted in 1813 by Baillie and Everard Home, has perpetuated the work and teachings of this man, and has drawn lessons from his career. So our materials for a study are abundant, and our accumulated knowledge of him is great.*

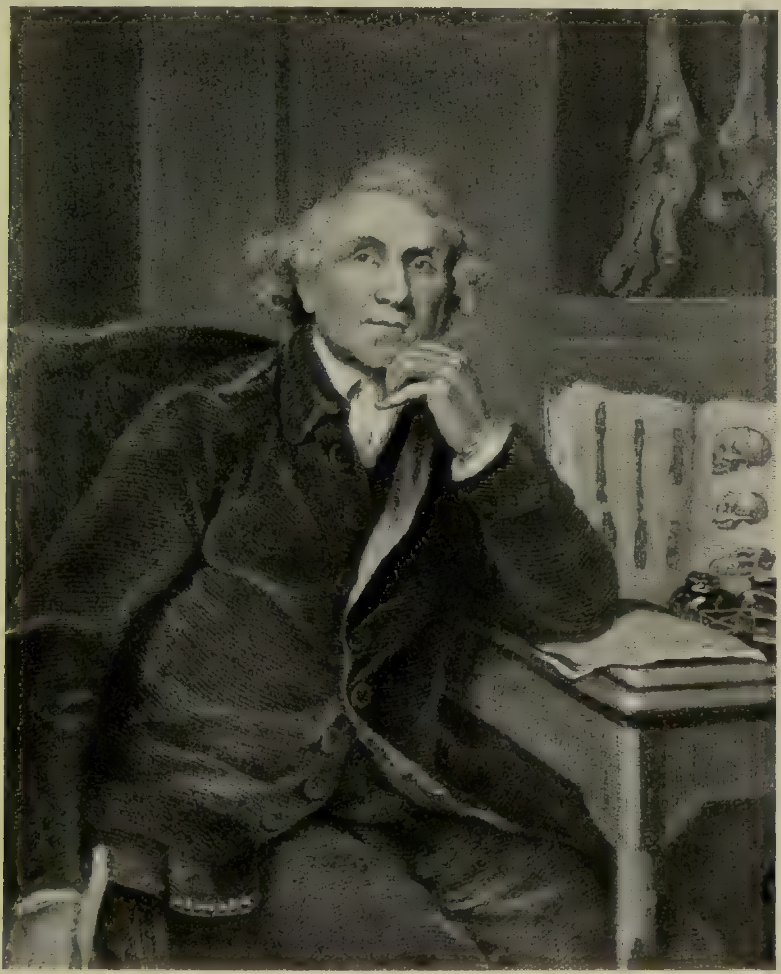

FIG. 4.—JOHN HUNTER.

John Hunter was a Scotchman, of good, robust, middle-class stock. He owed a good deal to his ancestry probably; certainly many of his immediate relatives distinguished themselves and showed the advantage of a clean and vigorous heredity.† Hunter's father is described as a small farmer living on his own estate, Long Calderwood, in the parish of Kilbride East, Lanarkshire, and there John Hunter was born on the 14th of February, 1728, as he himself always stated.* He was the youngest of ten, five sons and five daughters. James was the eldest of the family; William, the fourth son, was ten years senior to John.

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* The best "Life" is that recent one by Stephen Paget. In 1841 Drewry Ottley wrote a dreary account of John Hunter, prefixed to Hunter's Complete Works, edited by J. F. Palmer. Everard Home wrote a fragmentary and unreadable sketch of him for the first edition of the "Treatise on the Blood and Inflammation," 1794; and numerous writers, Sir C. Bell, Professor Owen, John White, and many authors of Hunterian orations, have dealt with phases of Hunter's life and work.

† Of his famous elder brother William we shall hear. His brother James, who died young, was a promising anatomist; his sister Dorothea was the mother of Dr. Baillie, the clinician, and of Joanna Baillie, the authoress.

It is always interesting to learn something of a great man's formative years, but of John Hunter's youth we know little. He seems to have been a vigorous, out-of-doors lad, devoted to rural sports; little given to books, but neither indolent nor unobservant. Indeed, how could he have been either? The tireless student and keen observer of the fifties could not well have come out of a dull and obtuse rustic of the forties. They say his mother petted him, which is true, doubtless, for was he not the youngest of ten? And at seventeen he was sent to Glasgow to help straighten out the affairs of a good-for-nothing brother-in-law—a bootless errand; but fools are not sent on such errands save by the Dr. Primroses of this world. There is no doubt, however, that Hunter received scant schooling, and that in his young manhood he was ignorant of books; but he was vigorous and ambitious, and his horizon was not limited to the home farm, for his elder brothers had gone out into the world, and of William he was proud from his youth up. A word about that particular elder brother.

William Hunter was born in 1718, and from childhood was destined for the church. He seems to have been an intelligent, sensible, attractive lad, eager in the pursuit of knowledge. At fourteen he was well advanced in his studies and was sent to the University of Glasgow. He became conspicuous there almost at once, but soon lost his purpose of being a clergyman. Meantime he had become intimate with William Cullen, six years his senior and a student of medicine. The intimacy bore fruit. Cullen, the future great teacher and clinician of Scotland, was astute even in his youth, and recognized William Hunter's abilities. So, upon Cullen's urging, Hunter entered on the study of medicine; from his nineteenth year to his twenty-second he was an inmate of Cullen's house. The next year, 1741, he spent in further study at Edinburgh, and then went to London to broaden his education and find a wider field for practice. It was a courageous undertaking and marks the man. Scotchmen were then few in London; George II was still living; Lord Bute did not come into power until eighteen years later, and Englishmen had not yet learned to complain that the King's favorite kept in his pocket all the offices and all the honors for his beggarly countrymen from beyond the border.

When William Hunter went to London he had to depend upon his little family estate, unusual gifts of brain power, a good education, and an introduction to Dr. James Douglas, an anatomist and obstetrician of some note. Douglas took a fancy to him at once; he received him into his house, made him tutor to his son, employed him as a prosector, secured for him a position as surgeon's pupil at St. George's, and procured for him first-class anatomic instruction under Dr. Nicholls. Douglas died, unfortunately, in the following year, but Hunter continued to live for a time in his family and rose rapidly in professional esteem. He soon began lecturing on surgery and anatomy, and proved himself one of the ablest and most popular teachers in England. In 1747 he became a member of the Corporation of Surgeons;[*] and in 1748 made a medical pilgrimage on the Continent. Then gradually he gave up surgery, to devote himself to obstetrics, anatomy, physiology, and general practice. In 1748 his brother John joined him in London, and in 1750 he received the degree of M.D. from Glasgow, his Alma Mater. The great Hunterian Museum of Glasgow was bequeathed by William Hunter to that University, and stands a splendid monument to its founder. He was now well launched upon his life-work, and there for the present we leave him; with this reflection, that his training and career were quite other than those of his more famous younger brother. He was an accomplished student and a university product. He was bred up in the best traditions of his profession. He was agreeable, spirited, interesting; an effective public speaker and a popular, inspiring, lucid teacher. Dignified, but apt, brilliant, and convincing in conversation, he was the friend of eminent men from his first coming to London. The best professional society frequented him, he became a member of learned bodies, and he held the respect and friendship of men of all ranks in that eighteenth century England.

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* The parish register gives *13th* February, 1728.

John Hunter, such a rough lad as we have seen, went up to London, to his brother William, in the autumn of 1748. He was twenty years old. He went to London of his own motion, stimulated by the growing reputation of his brother, and his brother received him kindly. One may fancy the intercourse of this ill-mated pair, but William seems always to have been patient and generous. Such discord as arose was John's doing mostly. The lad was a bear, and very much of a bear he remained to the end of his days—jealous, rude, outspoken, much self-centered, intolerant; of an ungovernable temper, given to very naughty language, frequent with oaths. In his youth boisterous, a hard drinker and worse, he was fond of horse-play and addicted to low company, I fear; but always kindly, generous, impulsive, a staunch friend, a good hater. His professional ethics were second-rate, his contempt of empty dignities and humbug was shouted from the house-tops. But he was as sound and unreasoning a Tory as his contemporary, Dr. Johnson; and his patriotism was unswerving and articulate. He hated fiddlers, laced ruffles, and Frenchmen.

John Hunter was not the first of the brothers to be attracted by William Hunter's work in London. A few years before this his eldest brother James had given up the law and entered William's dissecting room, where he came to be regarded as a promising anatomist, in the course of a year. But his health gave out; he returned to the home in Scotland and died there. John Hunter was physically sound at the outset—fortunately for him and for us. He plunged into his work with enthusiasm and he clung to it for forty-five years. His brother William found employment for him at once, preparing a dissection of the muscles of the forearm in anticipation of his lectures, which began three weeks later. The young man had had no previous acquaintance with his subject, but succeeded so well that he pleased his elder, who continued to encourage him in such studies, until at the beginning of the second session he was given charge of the dissecting room and the instruction of the pupils. So he went on. It is easy to see where he got his knowledge of anatomy, but just where he acquired early that broad knowledge of the allied sciences and of general medicine is not so obvious. Hunter used to assert, and writers have continued to tell, how he was without a training in letters, and was ignorant of what his predecessors and contemporaries did for the science of medicine. It is hard unreservedly to accept such statements, especially when we know that in later life he was a constant associate of learned men and a valued contributor to their discussions. We know too that in 1748 William Hunter was a companion of such men, who made his house a rendezvous. So the younger brother, from his twenty-first year, breathed an atmosphere charged with things good for intelligent minds, and doubtless was encouraged to read as well as to listen and to think. From the first, however, he did his own thinking; there can be no doubt about that, as one sees from his givings-forth. Few young men have acquired formed habits at twenty, so that we may believe these new friends helped to direct his energies and to stimulate his ambitions. At any rate his brother had no intention that he should remain a mere hack, and so the year after John's arrival the youth was placed under the tuition of the famous Cheselden at the Chelsea Hospital.

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[*] The Corporation of Surgeons, under a new charter, became The Royal College of Surgeons in 1800, and took over the Hunterian Museum from the government.

It is worth our while to glance a moment at Cheselden, one of the most eminent of that school of ancient surgery which was passing—for the passing of which Hunter himself was to be in great measure responsible. **William Cheselden** was himself a pupil of William Cowper, an anatomist and surgeon of Stuart times, and almost a contemporary of Sydenham and Locke. Cheselden was educated at St. Thomas's Hospital, became an able anatomist and a skilful operator while a young man, and for more than twenty-five years was regarded as the leading surgeon in England. He perfected the lateral operation for stone; he was the first to operate for artificial pupil; he was a member of the Royal Society, Surgeon to St. Thomas's, St. George's and the Westminster Hospitals, and the last warden of the Barber Surgeons' Company, immediately before the separation of the surgeons and barbers in 1744. Moreover, he was a kindly, accomplished, forceful, well-bred man—a gentleman of the old school, our fathers would have called him, an impressive character and a notable teacher. So there we have John Hunter, living with his brother William, the accomplished scientist, and learning to practice under Cheselden, the foremost surgeon in the country—truly an admirable school for a rude country boy.

The young man's experience of teachers was to be varied further. In 1751 Cheselden retired from the Chelsea Hospital, the year before his death. Accordingly Hunter transferred himself to St. Bartholomew's, where he became a pupil of Percival Pott, then in early middle age and vigorously at work. Pott was another admirable man, a man worth our acquaintance; a sound surgeon and a sound teacher, he was not yet known to fame, but was still in the enthusiastic, accumulating stage, when a man can do most for his pupils. He lived to be Hunter's rival and critic, but he always thought honestly and fought squarely.

Hunter remained with Pott for three years, and then, in 1754, became surgeon's pupil at St. George's, where he was appointed house-surgeon in 1756. Meantime, in 1755 his brother had entered him at Oxford, but he himself, at the age of twenty-seven, did not relish the idea and never kept his terms. The tale is often quoted that years afterward Jesse Foot, a surgeon and publicist, disparaged him for his ignorance of the ancient classics. Said Hunter, "Jesse Foot accuses me of not understanding the dead languages; but I could teach him that on the dead body which he never knew in any language dead or living." Hunter was never over-modest, and Foot was a foolish person, whose jaundiced "Life of Hunter" you shall read with groans.

Hunter chose St. George's because he had decided to be a surgeon, and because that hospital offered the best chance of future promotion. But he never neglected his anatomy in the midst of diverse other pursuits, and kept at work as pupil and tutor in his brother's dissecting room throughout those ten busy years. Hunter was as busy a man as Haller. We have seen Haller devouring books. However little or much Hunter did of that, he was a tremendous worker in his own line—laboratory research; and we shall hear how he was content with four hours of sleep, scanty rations, and little play. Even in those early years he was discovering things. Among other feats he solved the problem of the descent of the testis in the fetus, he traced the ramifications of the nasal and olfactory nerves, he tested experimentally the question whether veins could act as absorbents, he studied the formation of pus, and the nature of the placental circulation, and with his brother he practically proved the function and importance of the lymphatics.

All that brings us to 1759. He was now thirty-one years old; he had worked without ceasing in London for eleven years, and he broke down. That marks the end of his schooling and his youth. From now on we must think of him as the man of action—army surgeon, collector, investigator, teacher, writer, practitioner, and, toward the end, martyr to a fiery temper and a fatal, agonizing disease.

Hunter's breakdown in 1759 did not result seriously, though it disturbed his friends and alarmed himself. He was thought to have incipient phthisis, so he determined to find work and a residence out of England for a time. In the following year he secured a commission as staff-surgeon to Hodgson and Keppel's futile expedition to Belleisle—the same expedition which Thackeray has rendered forever comic in his account of Harry Warrington chased by the dragons. Hunter returned unscathed and the next year went to serve with the English forces on the frontier of Portugal. We cannot stop to learn of his army life except to note that for four years he was with the troops and acquired a great experience in the treatment of gunshot wounds. He came to regard the presence in the tissues of a bullet as not in itself harmful, thus coinciding in opinion with his predecessor Paré. He was too intelligent and diligent a man to content himself with the mere discharge of his duties, arduous as they were, but was continually engaged in physiologic and other researches. He studied the conditions of the coagulation of the blood, he continued his old anatomic work, and he collected a great mass of memoranda on inflammations. In those years, too, he began his exhaustive researches into the habits, functions, and structure of plants and animals. He learned that digestion does not go on in snakes and lizards during hibernation, and that the creatures will die in that season if they are put through vigorous movements; so he was led to an interesting conclusion which he applied to his human patients; namely, that if the powers of a part are diminished through gangrene or local necrosis, stimulants are dangerous, since they "increase action without giving real strength." Soon after his return from Portugal he wrote out a catalogue of his specimens, and recorded notes of about two hundred normal and diseased structures. He retired on half-pay in 1763, at the end of the Seven Years' War, but those four years were not the least important for health and progress in his life, and he was wont to look back on them with satisfaction. The experience reminds one of what Darwin, Huxley, Beaumont, Reed and other distinguished men have known. There is place in the public service for scientific work of the highest type, as we have learned.

We find Hunter, then, at the age of thirty-five, in London, with a start still to make, on a short allowance, but splendidly equipped in courage, ability, and training for the task before him. He proposed to be a practising surgeon; meantime he must live. So he began teaching anatomy and operative surgery to private classes and renewed his acquaintance with the resurrection man. Such teaching was his forte. He never enjoyed formal lecturing; indeed, when he took up that work later, he did so with dread. He began each course with embarrassment and hesitation, and used to fortify himself with a large dose of laudanum before his introductory lecture.

Scant practice and a daily class would have left most men with abundant leisure, but Hunter had no leisure in life. He went on at once with the further study of comparative anatomy, and for subjects obtained animals dying in the Tower menagerie and in traveling zoölogical shows. He worked even when he was ill. They tell how he ruptured his tendo Achillis, and while so disabled experimented on the tendons of dogs. He devised the familiar operation of subcutaneous tenotomy, killed the animals at various stages of their convalescence, and through those studies ascertained the method and course of tendon healing. Out of such work grew the modern operations of that nature. In 1767 he was made a member of the Royal Society—a fact noteworthy, since he had as yet published but one brief paper, and his brother William did not receive the honor until several years later. Evidently the great ability of the younger man was already making itself felt. The next year, 1768, he was appointed surgeon to St. George's Hospital and became a member of the Corporation of Surgeons, five years after settling to practise; and now he established that routine of daily life for which he was remarkable to the end. All great scientists have been workers, but Hunter worked in a fashion unknown even to our incessant modern life. He rose at five o'clock, and without waiting for a decent toilet hastened to his private dissecting room. There he worked until nine o'clock, when he snatched a hasty breakfast. He was methodical. From breakfast time until twelve he received office patients, and at twelve promptly, no matter who waited, he went out to make professional calls and his hospital visit. He returned home at four, and dined. He ate abstemiously and, for the last twenty years of his life, drank no wine. After dinner he slept for an hour, and at half-past five went to work again. Those evening hours were his most effective hours. He kept at it incessantly until after midnight, going to bed between one and two in the morning. He must have been a cheerful companion for his wife; for he married, of course, and in some fashion managed to beget and rear children. Mrs. Hunter was the daughter of a Mr. Home, a struggling army surgeon, and for this lady, in his early poverty, Hunter had to wait several years. He married her finally against the protests of his worldly-wise brother, whose opposition to the match is said to have been the beginning of that breach which finally separated the two men. John Hunter's wife was a good wife to him, though his selfishness and rough manners must have tried her sorely. She was a pleasant, social body, given to cakes and ale, and rather partial to those fiddlers and Frenchmen whom her husband abominated. Here is a sombre tale of social misadventure: "On returning late one evening, after a hard day's fag, he unexpectedly found his drawing-room filled with musical professors, connoisseurs and *other idlers*, whom Mrs. Hunter had assembled. He was greatly irritated, and walking straight into the room addressed the astonished guests pretty much in the following strain: 'I knew nothing of this kick-up, and I ought to have been informed of it beforehand; but as I am now returned home to study I hope the present company will retire.' "* He was a good old-fashioned British husband, and his sprightly wife remained faithful to him, though he bullied her while he lived and left her penniless when he died. Mrs. Hunter had a younger brother, Everard Home, twenty years Hunter's junior. The lad became a member of their household; studied surgery under his distinguished kinsman, was taken into his confidence, was made his assistant, partner, and executor, grew to fame on his fame,—Home was not without ability of his own,—and made himself forever infamous, long afterward, by burning a great collection of the Hunterian manuscripts in order to conceal his own literary pilferings—a scandal with which scientific London blazed in the early years of the last century.

In 1768, then, John Hunter found himself well established; he moved shortly afterward into his brother's former house, and began to take house-pupils—many of them afterward famous. Of such pupils were Jenner, Guy, our own Physick, Lynn, and Carlisle. At St. George's he had Abernethy, Cline, Earle, and Astley Cooper, and he taught those young men to work as he worked himself. Early in his career Hunter recognized that, as yet, comparatively little had been done to explain the nature of disease, its significance, its relation to health, its progress, and its classification. Again we are confronted with the problem of Hunter's ignorance or familiarity with the accomplishments of other workers. Of course, he must have known the broad outlines, the common property of all physicians of his time, but he often seemed to feign ignorance, or, what is more probable, he distrusted published conclusions, and had pretty steady contempt for the capacity and observations of his fellows; not that he trusted himself implicitly, though he thought well of John Hunter; but he used to tell his pupils not to refer to what he had said the year previously, for he reserved to himself the right of changing his conclusions. At any rate, Hunter, unlike Paré, perceived that medicine was in its infancy, and he undertook the stupendous task of revolutionizing ancient methods of study and launching science anew upon sound and rational lines. He began with fundamentals; he insisted upon a review of anatomy; and he taught that a thorough knowledge of embryology is essential to an intelligent pursuit of anatomy. Not only that, but he perceived the significance of the structure of animals of varying types, and of plants too. He had more than a suspicion of the evolution of species and their origin, and insisted that a foundation in medical knowledge could be acquired only from an exhaustive study of comparative anatomy and of animal and vegetable life. In such studies and in such teaching he was unwearied. Read his works and you shall find an astounding variety of evidence that he had anticipated a thousand modern discoveries and had constructed hypotheses which have been adopted since as some of the important theories of recent research. Not content with such work, he was indefatigable in his investigation of physiologic problems in man, animals, and plants. In his own laboratory and with the rough tools at his command he performed experiments and reached conclusions not unworthy of a Harvey, a Haller, a Spallanzani, a Bichat, or a Claude Bernard; and he inspired with a like diligence and enthusiasm the few choice spirits who had the wit to appreciate his greatness and the courage to follow his lead. They were young disciples. Among his contemporaries he had no following. What great man's contemporaries ever did become his followers? Maturity does not seek novelty. The prophet must have young men about him if his words are not to fall fruitless. Were progress to depend upon a man's contemporaries, we should be in the stone age still. New life, new blood, fresh enthusiasm, and vigor are needed for advance. The "judgment of experience" expresses the recognition of familiar conditions; and experience is palsied in the face of novelty.

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* Ottley.

Fundamental work was Hunter's great work. It is for such that we hold him in the front rank of all our benefactors. He saw the meaning of science more clearly than any man who had lived; and he had the genius to make others see that meaning. That marks him as it marks the few rare spirits of his kind to whom men have given ear.

Hunter was not infallible. He made many mistakes; for he strove much and often, and such constant strivings end sometimes in error. But he was luminous and articulate to show the way, not hoping in one short life to reach the goal of all knowledge, but confident that from his Nebo his successors should advance upon the land which to him was vouchsafed as a vision only.

Hunter's method was rigid adherence to deduction founded upon observation and experiment; and his studies embraced an enormous field. Let us pass in brief review some of his better known contributions to science: In 1772 he published his first paper in the "Philosophical Transactions," an essay on post-mortem digestion of the stomach, in which he explained that phenomenon as a result of the action of the gastric juice. In 1771 and 1778 appeared his essays on the teeth, whose natural history was explained and their diseases exhaustively considered. The work was an authority for three generations. In 1774 he read before the Royal Society a paper on birds, describing their manner of breathing; and a paper on the stomach of the Gillaroo trout. During these same years he was busy with investigating the temperatures of animals under varying conditions, and his letters to Jenner, his constant correspondent, describe his elaborate clinical thermometer in a fashion worth reading. Such investigations led to a delightful paper, which he read before the Royal Society in 1778, on the "Heat of Animals and Vegetables."

Two years afterward, in 1780, Hunter presented to the Royal Society a paper which precipitated a bitter quarrel with his brother William, a quarrel which was healed a few days only before the elder's death, three years later. John Hunter's paper dealt with the structure and circulation of the placenta, with facts which he claimed to have discovered and established many years before, when working in his brother's dissecting room. Now, William Hunter had published the same observations in his work on the "Gravid Uterus" in 1775. The lie was given and returned publicly between these eminent men, and the Royal Society refused to print John Hunter's paper. He acted badly, whatever the rights or wrongs in the case may be. In this same year of 1780 Hunter read before the Society an account of a fetus, dead of smallpox, and a paper on the change of plumage in non-breeding hen-pheasants. In 1782 there followed an essay on the organ of hearing in fishes.

Lectures, essays, letters, flowed from him continually during these years, but it was in 1785 that he made the observations and performed the operation for which he is best known to students of surgery—Hunter's operation for aneurism. The story is interesting and illustrates the man. He happened in that year to be studying the mode of growth of deer's antlers. In July he had a buck caught, and tied one of its external carotid arteries. He observed that the antler which was nourished by this vessel became cold to the touch, and he debated whether this antler would be shed in due course or would be retained longer than usual. To his surprise he found, two weeks later, that the wound was healed and that the antler was again warm and vigorous. He supposed the ligature might have slipped, so he had the animal killed, when on examination he was interested to discover that the ligature held, but that, through anastomosis and enlargement of small vessels above and below the occluded part, normal circulation had been restored to the growing antler. From this observation he was led to the conclusion that "under the stimulus of necessity" the smaller arteries are capable of rapid increase in size to perform the function of the larger.

Soon afterward he had an opportunity of applying to a human patient this newly discovered law. There entered the wards of St. George's Hospital a man suffering from advanced popliteal aneurism, and in approaching the case Hunter debated whether to employ the old method of Antyllus,—dissection and double ligation,—or to follow the practice of Pott, amputation well above the aneurism, declared by Pott to be the only safe method. Hunter was conservative in his practice. He abhorred meddlesome surgery, and used the knife when other means had failed only. He felt the operation of Antyllus to be dangerous, and the method of Pott to be needlessly severe. He argued, however, that it would be reasonable to tie the femoral artery at that safe point where Pott would tie it in an amputation. He would not amputate, however, but would count upon the anastomosis for restoring circulation to the leg. Accordingly, he acted upon this reasoning, and with success. He tied the vessel in that intermuscular space known since as Hunter's canal, and was gratified after several hours to find that the temperature of the foot had not fallen, but had risen above the normal. The patient progressed satisfactorily, and six weeks later, with a sound and useful leg, was discharged from the Hospital. The fame of this operation went abroad and aroused commotion. Promptly Frenchmen and Italians claimed priority for their countrymen, while many English surgeons, headed by the veteran Pott, denounced the procedure as dangerous and unwarrantable. But it gained ground and became accepted in spite of loud words. Wise men waxed enthusiastic over it, and the Italian Assalini, who saw it first performed, testified that it "excited the greatest wonder, and awakened the attention of all the surgeons in Europe."

In 1783 Hunter had taken a leading part in establishing the "Society for the Improvement of Medical and Chirurgical Knowledge," and several of his papers were read subsequently before that body. In that same year he read to them an admirable paper on "Phlebitis," the first paper we have which gives a satisfactory explanation of that affection; and in 1786 he gave to the world his famous book "On the Venereal Disease," a book long awaited by the profession, and an authority for fifty years thereafter. A few months subsequent to its appearance he published his work on the "Animal Economy," a collection of important papers consisting of many admirable anatomic descriptions, and accounts of numerous original researches in physiology. In 1787 he gave to the Royal Society a paper on the "Wolf, Jackal, and Dog," and a second paper, well illustrated, on the structure and physiology of whales.

In those years Hunter was overwhelmed with a thousand cares, and suffered much in health, so that his writings were few and at long intervals after 1787. In 1792, the year before his death, he contributed to the "Philosophical Transactions" a paper on bees, the result of his observations on the hive-bees, studied for more than twenty years. His last printed book, a book regarded at the time as the most important of his productions, was posthumous, the final editing being done by Everard Home; its title, "A treatise on the Blood, Inflammation, and Gunshot Wounds, 1794."

Thus, in a few words, I have told something of the more notable things which Hunter did, but the story is very bare. It would be interesting to look out with him upon the world in which he lived and learn something of what other men were doing. The influences which bore upon him, and the condition of Europe in that last half of the eighteenth century, were vital and remarkable. Politics and literature, philosophy and science, were undergoing profound impressions. Hunter was no closet student, but a man keenly interested in what was doing, and for long much in the eye of the scientific world. All this must be a passing thought, however, but we may glance again at Hunter's life, his later years, and bring our story to a decent close.

One recalls certain facts not altogether agreeable or attractive, minor faults of temper and habit. His body was grievously overdriven by an iron will, so that there resulted ill health and a vicious temper, with which he struggled for years. Certain it is that he suffered from angina pectoris, and found little relief. Overexertion brought on frequent attacks, and outbreaks of passion or the attempts to suppress passion were a constant dread to him. So far back as 1772 he began courses of systematic lectures which were a severe strain upon him, owing to his painstaking method and labored delivery. He published his lectures later—a standard work of immense learning and rare originality.

In spite of his labors and fame he never made much money, and what he did make went for specimens and apparatus. He was one of the greatest collectors ever known, and scoured the world through friends and messengers for the flora and fauna of all lands. Dozens of his letters to Jenner deal with the habits of the cuckoo; he sent a special expedition to the Arctic for specimens of the whale and paid five hundred pounds for the skeleton of an Irish giant.

I have said that it was Hunter's conception and teaching of science which mark him the great man, but to his immediate successors and to the casual reader of today he is best known for his museum. The Hunterian Museum was the means to an end, but it was a magnificent means. Measured in bank-notes, it cost him upward of three hundred and seventy-five thousand dollars. After his death it was sold for seventy-five thousand.

Hunter seems to have valued money as of service only to enrich his collection. Up to 1780 his income ranged between five and ten thousand dollars a year. For a few years before his death it reached twenty-five thousand, and in one year more than thirty thousand dollars. Most of his contemporaries regarded his love of collecting as an eccentricity and his devotion to science as almost a mania. Few perceived the drift of his biologic researches, and his investigations in comparative anatomy were looked upon as works of unprofitable curiosity. Even his friend, Sir Joseph Banks, the president of the Royal Society, wrote, three years after

Hunter's death, that he did not believe the Hunterian collection to be "an object of importance to the general subject of natural history, or indeed to any branch of science except to that of medicine."

The collection is estimated to have contained 13,682 specimens: In the physiologic department, 7295; in the pathologic, 2678; and 3709 fossils. In the year 1800 it was acquired by the Royal College of Surgeons, since when it has been greatly increased, thanks largely to the efforts of its distinguished line of custodians, William Clift, William Home Clift, Richard Owen, J. T. Queckett, and William Fowler.

A writer* has defined the scope of these labors of Hunter as the explication of the various phases of life exhibited in organized structures, both animal and vegetable, from the simplest to the most highly differentiated. Hunter did not employ comparative anatomy in subservience to the classification of living forms, as did Cuvier, but in order to ascertain the principle which animated and produced those forms—a principle by virtue of which it appeared that all forms were allied to himself. He was continually asking himself, In what does life consist? He came to teach that "life is a principle independent of structure, most tenaciously held by the least highly organized beings." Abernethy says he perceived life to be "a great chemist," a power capable of manufacturing a variety of substances into one kind of generally distributed nutriment, and of furnishing from this a still greater variety of dissimilar substances. Hunter found, in short, that there exists in animals a latent heat of life set free in the process of death. "Mere composition of matter," said he, "does not give life; for the dead body has all the composition it ever had; life is a property we do not understand." As a bar of iron may gain magnetic virtue by being placed for a time in a special position; so, perhaps, the particles of matter arranged and long continued in a certain posture eventually gain the power of life. "I inquired of Mr. Hunter," writes Staple, "if this did not make for the exploded doctrine of equivocal generation; he told me perhaps it did; and that as to equivocal generation all we could have was negative proofs of its not taking place. He did not deny that equivocal generation happened."

Hunter held certain interesting views on geology. In water he recognized the chief agent for producing terrestrial changes; but he held untenable the popular notion that Noah's deluge might account for the marine organisms discovered on land. From the diversity of the situations in which many fossils and allied living structures are found he was led to infer that at various periods there had taken place not only repeated oscillations of the level of the land, lasting thousands of centuries, but also great climatic variations. The following striking paragraph of Hunter's is from Butler's essay: "If we were capable of following the process of increase of the number of the parts of the most perfect animal, as they first formed in succession from the very first to its state of full perfection, we should probably be able to compare it with some of the incomplete animals themselves, of every order of animals in the creation,—being at no stage different from some of those inferior orders; or, in other words, if we were to take a series of animals from the most imperfect to the perfect, we should probably find an imperfect animal corresponding with some stage of the most perfect." In spite of involved phrasing, this thought, coming to us out of the eighteenth century, is supremely interesting.

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* F. H. Butler.

Such were some of Hunter's labors and teachings. Like every genius he kept himself young, and projected himself beyond his generation. As he advanced in years and grew to fame his fits of temper and his intolerance of opposition increased upon him. It was his temper that killed him. He had become unavoidably concerned with medical politics—a field in which he was not calculated to shine. There came to be bad blood between himself and his colleagues at St. George's because he announced that they were neglecting the surgical pupils and that thereafter, as he was doing most of the work and attracting most of the students, he should not turn in the fees to the common purse, but would keep them for himself. The governors of the Hospital ruled against his decision, and provided, in addition, that thereafter no student should be admitted who had not been educated in medicine. This last rule seemed to be aimed at Hunter. It irritated him particularly because, soon after, there came up to London two young Scotchmen, ignorant of the new law but seeking to be taken on as his pupils. He explained to them the situation, but promised to do what he could. For that purpose, on the 16th of October, 1793, bent on seeing his Scotchmen through, he attended a meeting of the Hospital Board. Ottley tells the story: "Arrived at the Hospital he found the Board already assembled, and entering the room presented the memorial of the young men, and proceeded to urge the propriety of their being admitted. In the course of his remarks he made some observations which one of his colleagues thought it necessary instantly and flatly to contradict. Hunter immediately ceased speaking, retired from the table, and struggling to suppress the tumult of his passion, hurried into the adjoining room, where, with a deep groan he fell lifeless."

It is a pathetic and tragic scene. One fancies the winged words that may have passed, the taunt of that nameless colleague, who was probably in the right, the fury of Hunter, who was probably in the wrong. Rembrandt should have lived, and added that picture to his collection. The fate of those two disappointed young Scotchmen has not been told.

Look back the hundred and thirteen years which have passed since Hunter died; think what his life means for science and what is the estimate placed upon it by the average physician of today. The Englishmen have done their best for him, to be sure. Two of his influential relatives established the annual Hunterian Oration, which survives; but in the profession at large he is little more than a myth. A recent publicist says of him, that he stands for a book of surgical lectures, a treatise on venereal disease, and the operation for aneurism. He stands for far more. Those things were by-products dropped from the seething laboratory of his brain. He means for us the first and the greatest English-speaking exponent of proper scientific research. He is the father of us all, physicians, surgeons, laboratory students, for he wrought mightily in all fields.

John Hunter inspired little personal affection or devotion, though he inspired admiration and respect, for his was a vast genius. His disciples recognized the genius; few loved the man. With him it was not, as with Hippocrates, or Paré or Boerhaave or Haller. It was a fiery soul—onrushing, fierce, eager, intolerant, unsparing of others as of himself; the body exhausted out of season, the task unfinished; but his works do follow him. In modern days only have we come to see that sound knowledge and appreciation of science must be sought along those lines laid down through toil, criticism, and weariness by the indefatigable John Hunter.

AMERICAN SURGERY.

It is interesting, before going on with the narrative of world surgery, to glance more particularly at the progress of surgery in this country, so far as one may in brief retrospect and without becoming involved in a discussion of the achievements of living men.

The best early American surgery grew out of English surgery, with John Hunter as the prophet, and as our best surgery was for nearly a century dependent on the teachings of Europe, it may be divided conveniently into three eras: the Hunterian era, the middle or French era, and what we may call the German-American era. Let us note, then, some of the great American surgeons in each of these periods and recall a few of their important deeds, but with this prefatory consideration; until within recent years American life has furnished little opportunity for the closet student and the laboratory student of science. Some great surgeons have lived and flourished among us, but the stress of life and the circumstances of their being have forced them into practical work, into personal relations with their fellows. With a few exceptions they have created no great new thing, but they have been able exponents of borrowed work, and they have been daring practical operators of the highest type. It is a story of great clinicians.

John Jones.—American surgeons must look back to John Jones, of New York, as the first of their eminent professional forebears. Jones was born in New York city in 1729, so that he was a contemporary of Washington. He did his work in his native place, and there he died in 1791, at the age of sixty-two. It is a forceful, sterling character, of value in those days to the patriot cause in arms. Jones may be called a disciple of the Hunterian era, though in fact he was but one year younger than John Hunter himself. But Hunter and Jones studied in the same schools and knew the same masters, and the younger man came to be influenced greatly by the work and teaching of his more famous English contemporary. Jones studied in London under Percival Pott; in Paris under the great French reformers, Petit and LeDran, and in Edinburgh under the elder Monro. He became distinguished in colonial annals as surgeon to the troops in the old French War of 1758, and then, upon the foundation of King's College, he was made the first Professor of Surgery, in 1767. The chroniclers note of him that he was the first American to perform the operation of lithotomy.

John Jones' most conspicuous work, and that for which he is commonly quoted, is his book entitled "Plain, Concise, Practical Remarks on the Treatment of Wounds and Fractures," New York, 1775, reprinted at Philadelphia in the following year, with Van Swieten on "The Diseases Incident to Armies and Gunshot Wounds." This little book became the *vade mecum* of Continental surgeons during the Revolutionary War. Jones attempted little more in it than to condense the teachings of Pott and LeDran; but there are a few notes of originality, the most conspicuous being a case of trephining in delirium, eighty days after a slight head injury. The dura was opened and drained and the patient promptly recovered.

After the war, Jones went on with his teaching and practising until his death. He was a useful and honorable man, an admirable type of the best of that long line of surgeons with whom we have to deal.

William Shippen, Jr.—The second of our early surgeons, a contemporary of Jones, was William Shippen, Jr., of Philadelphia. Like Jones, and like most of the men of his own and the succeeding generation, he was admirably educated in foreign schools. Shippen was born in 1733 and studied in Leyden, Edinburgh, and London. He was a special pupil of William Hunter. To us he is memorable for two things: with John Morgan he founded the medical department of the College of Philadelphia (later the University of Pennsylvania) and he served with distinction as Physician-General to Washington's armies from 1777 to 1781. Next to Morgan and Rush he was probably the most distinguished American physician of his generation, and the conduct of his department during the war was admirable and creditable. Though an able and popular teacher he seems to have added nothing of importance to the science or art of surgery.

John Warren.—Somewhat younger than the two distinguished representatives of New York and Philadelphia was John Warren, of Boston; indeed, he belongs almost to another generation. Warren was born in 1753, a younger brother of that General Joseph Warren, famous as a hero of Bunker Hill. Unlike Jones and Shippen, Warren found his education entirely in America; but, in spite of this apparent disadvantage at the start, he is eminent in our annals as a great clinical teacher and surgeon, and as the founder of the Harvard Medical School. So one observes that these three men, our first distinguished surgeons, living haply in different towns, are notable chiefly as founders and first surgical professors in our three oldest and most famous medical schools. Warren served with distinction as hospital surgeon during the Revolution. For some months before the conclusion of peace he was in charge of a great military hospital in Boston, where he found material and opportunity for teaching and operating, and it was almost immediately after the dissolution of this hospital that he assisted in the foundation of the medical school, in which he was appointed to the chair of anatomy and surgery, where he labored until his death in 1815.

American surgeons will remember that we owe more than a casual glance at these three men. In the straitened and difficult circumstances of our colonial and early national life, the foundation of schools and hospitals was a gigantic task; for be it noted that hospitals often followed or were associated with the foundation of schools. In England hospitals long antedated schools, and out of hospitals schools arose. Our surgeons, living in sparsely settled communities, where extreme poverty was little known, were able to bring about the foundation of hospitals with difficulty; but the need of proper medical education appealed more directly to their constituents, so with the beginnings of our national life schools sprang up here and there, and with the development of a more complex civilization, hospitals, too, came to find their place.

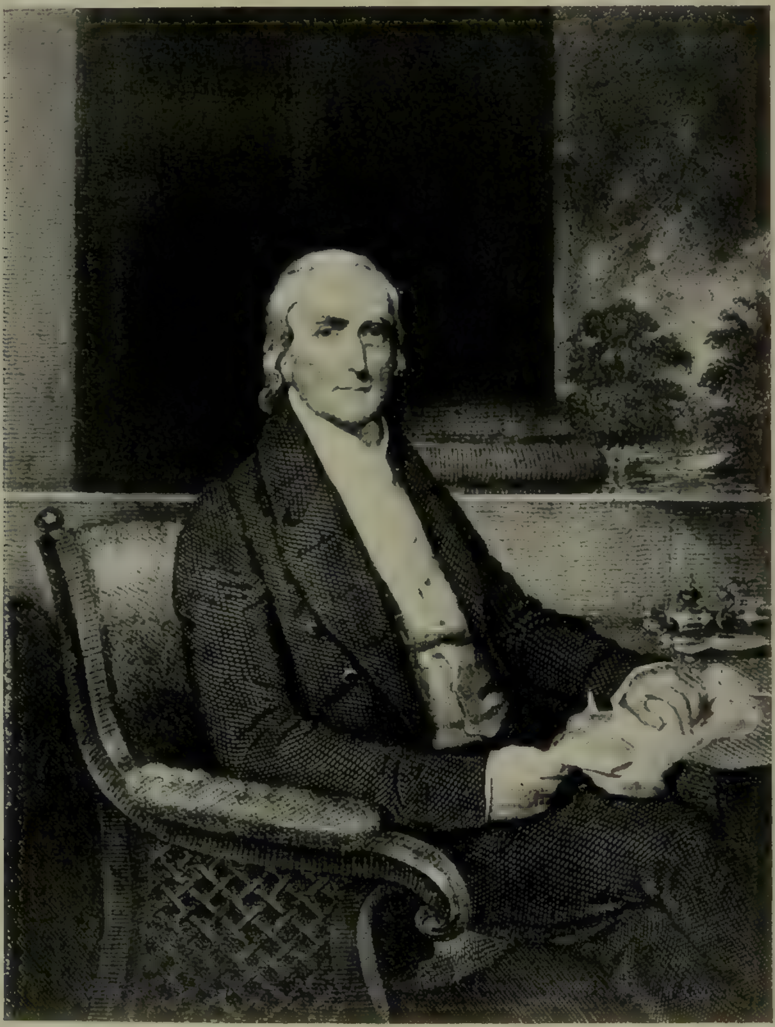

FIG. 5.—PHILIP SYNG PHYSICK.

Partly, perhaps, on account of the paucity of schools and hospitals, and partly owing to the strenuous forward march of our civilization, behind which schools and hospitals lagged for many years, we find that all of our great early surgeons are not to be discovered in the medical centers. The seaboard towns furnished admirable and well-equipped practitioners; but able practitioners were found on the frontier also, and when we come to study the surgical annals of the last century, we encounter records of accomplishment not alone in the Eastern States, but we hear of voices raised in the western wilderness.

Philip Syng Physick, called the Father of American Surgery, is perhaps the most widely known surgeon in our annals of the last century. Certainly he should head the Hunterian era among us; for he was a personal friend and pupil of John Hunter and his life was dedicated to practising and teaching the principles of that great man. Physick was born in Philadelphia in 1768; was educated in Edinburgh and London and became surgeon to the Pennsylvania Hospital in 1794. In 1805 he was appointed to the chair of surgery in the University of Pennsylvania. Unfortunately, he contributed little to the literature of surgery and his fame rests on the tradition of his operations, the tales of his pupils, and the compend of his practice, published by his nephew, Dorsey. Physick maintained the unfortunate sedentary habits common to his generation, and encouraged thereby a chronic dyspepsia, a recluse temperament, and a somewhat morbid view of life. He is not an interesting character; but he was a profound student, a clear-headed practitioner, and an ingenious mechanician. In a multitude of ways he improved the technic of American surgery, and seems to have done faithfully and well whatever he attempted. He bettered the famous long splint of Desault; he performed internal urethrotomy for stricture; he employed the seton for ununited fractures; he invented the stomach-pump for cases of poisoning; he bled to depletion preliminary to reducing long-standing dislocations; he was a lithotomist, and at the last, in his terror lest his body be dissected, he provided that the corpse should be guarded for many weeks after his decease.

Wright Post.—After Physick there are two New York surgeons, Post and Mott, who are worthy of our study. Mott's is the greater name, but Post was the first New York surgeon of eminence in the nineteenth century. Wright Post was born in New York in 1766, nine years before the outbreak of the Revolution. He studied in London under Sheldon, and six years after his return home was appointed Professor of Surgery in Columbia University, in 1792, when he was but twenty-six years old. He taught and practised for thirty years longer and died in New York in 1822. The man is notable as a daring operator and skilled anatomist. He first, in this country, in 1796, performed Hunter's operation for aneurism of the femoral artery; in 1817 he ligatured the subclavian artery in its outer third, and in 1813 he ligatured successfully the external iliac artery—the second operation of its kind to be performed. His name is familiar, and was famous among New Yorkers one hundred years ago.

Valentine Mott was nineteen years junior to Post, and lived down to modern times. I know of no man more famous among New York surgeons. His life is an inspiration to students; but we have space for the briefest outline only. He was born on Long Island in 1785. He died in 1865, the last year of the Civil War. After his graduation in medicine from Columbia in 1806, Mott studied for some years in London, part of the time under Astley Cooper, and returned to this country in 1810. He was appointed Professor of Surgery in the Columbia School and retained the chair when that school was merged into the College of Physicians and Surgeons, in 1813. He was a teacher all his life and in sundry schools. His private classes were large and lucrative. In 1826 he was for a time Professor of Surgery in Rutgers College; and again in the College of Physicians and Surgeons, resigning in 1834. In 1840 he became Professor of Surgery in the University of New York, and finally, in 1852, retired with the title of Professor Emeritus; even then he continued his annual course of lectures until his death, at the age of eighty.

To the student of surgical history the reason for Mott's permanent fame are not altogether clear, but among his contemporaries he was regarded as an heroic figure. He was a man of distinguished presence, of instant popularity, courtly, kindly, polished, with a sound and wide-grasping mind, highly cultivated under the best teachers, with a far-reaching ambition and an intimate knowledge of professional needs in our developing American life. He did a great number of things and he did them boldly and skilfully. His fame became established through his ligature of the innominate artery, for the first time on record, in 1818. The case must be counted as unsuccessful, though the patient lived several weeks, and it is worthy of note that the first successful case of the kind was in the hands of another American surgeon, A. W. Smythe, of New Orleans, who performed his operation in 1864. Mott is known to us especially for his work on aneurisms. He tied the common iliac in 1827, and during his career he was able to record the ligature of 132 of the great vessels, including 8 of the subclavian, 51 of the common carotid, 6 of the internal iliac, 57 of the femoral, and 10 of the popliteal. In 1828 he removed the entire clavicle, for osteosarcoma, and he was wont to refer to this as his Waterloo operation. In 1821 he excised the right half of the lower jaw, unaware at the time that a similar operation had been performed in 1810 by W. H. Deadrick, of Tennessee. It is needless to rehearse the multitude of Mott's performances. They were regarded as epoch-making; but enough has been said to illustrate the man and the distinction of a character which is still numbered among the greatest of American surgeons.

Ephraim McDowell deserves our gratitude; his life was romantic and his fame posthumous. He was born in Virginia in 1771, and removed when a boy to Kentucky. With the exception of one year, 1793, spent in Edinburgh under John Bell, his life was passed in Kentucky, where he practised at Danville. In 1809 he performed ovariotomy. In 1817 he reported this case with two others in the Philadelphia "Eclectic Repertory,"* but the world regarded him not. It was only in later years that the greatness of his performance became recognized, and now he has long been known as the pioneer ovariotomist.

With McDowell one couples **Nathan Smith,** another frontiersman in American surgery, though he lived in New England and was widely known as teacher and physician. Smith was born in 1762 in Massachusetts, and grew to manhood a farmer's boy in Vermont. Then ambition seized him; he returned to his books, studied under a preceptor, was graduated in medicine from Harvard in 1790, and founded the Dartmouth Medical School. There he did almost all the teaching for many years, occupying what Holmes has wittily described as not a "Chair" but a "Settee of Professorships," until he had placed the department upon a strong foundation, when, in 1813, he accepted the chair of medicine and surgery in the newly established Yale Medical School, at New Haven. His fame rests upon his founding of Dartmouth, his teaching of clinical medicine,—notably his exposition of typhus fever,—and especially upon his work as a surgeon; for he, too, was a pioneer ovariotomist. He operated upon his much quoted case in 1821, ignorant of McDowell's work. He tied off and dropped the pedicle, which McDowell had not done, and his patient recovered. Smith's life was crowded with teaching, writing, and practice; and he left a reputation which has endured.

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* "Eclectic Repertory and Analytic Review," vii, p. 242. Philadelphia, April, 1817.

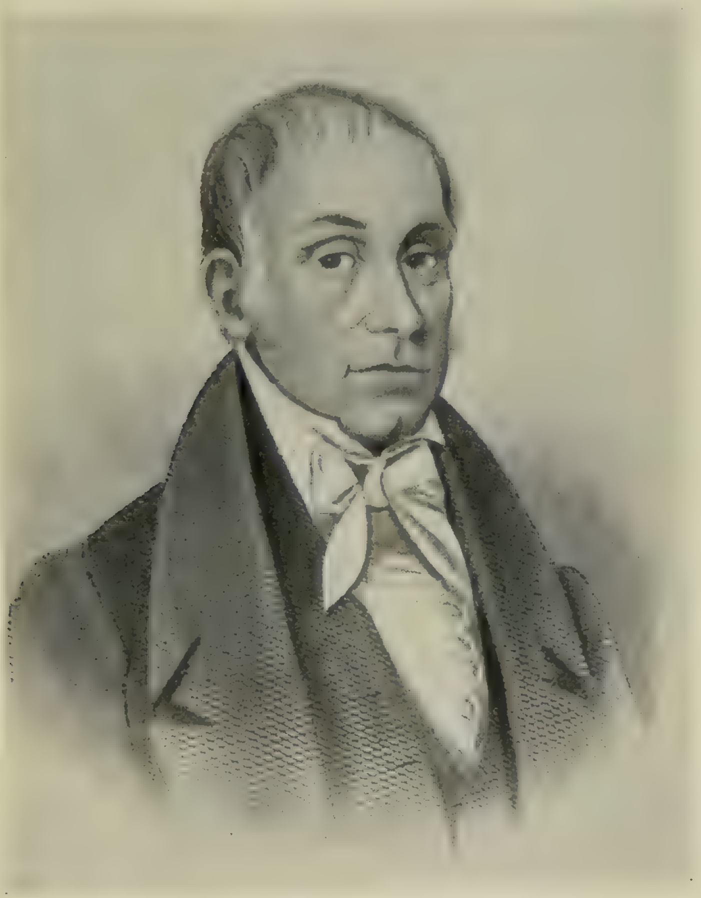

FIG. 6.—EPHRAIM McDOWELL.

John Collins Warren.—After Physick and Mott, John Collins Warren is probably the most eminent American representative of our Hunterian era. He was the eldest son of John Warren and was born in Boston in 1778, four years before the founding of the Harvard School. Unlike his father, he received a foreign education, studying in Paris and Edinburgh, and in London under Astley Cooper. For more that fifty years he was the leading surgeon of New England. He was Professor of Anatomy and Surgery at Harvard, and with James Jackson founded the Massachusetts General Hospital in 1811, where he served as senior surgeon for more than thirty years. As time develops and we get a better perspective of Warren's life, we are coming to appreciate his great service to American surgery and to American medical education. He was one of the early presidents of the American Medical Association. As an operator he was exact, painstaking, rapid, and successful. His observations were sound, his writing lucid and instructive. He was one of the first in this country to excise the hyoid bone, to perform osteoclasis, excision of the head of the humerus, staphylorrhaphy, and external urethrotomy, and his work on the excision of tumors is notable. He organized a great hospital on lines and with methods which persist to this day, and, most important of all, he first dared to employ ether anesthesia in surgery, in the year 1846. The story of the great ether controversy—who discovered anesthesia?—is more than a twice-told tale, and needs no rehearsing now. A word, though, about the significance of that same anesthesia. Before its time surgical operations were dreadful things—a hell to patients and a purgatory to operators. Indeed, most of the great and humane surgeons hated and dreaded severe operations. John Hunter is often quoted as asserting that an operation is a confession of failure, and is the last resort of our art. Cheselden, Brodie, Warren, Liston, Simpson, and dozens of others bore similar testimony. The frightful shrieks from ancient hospital amphitheatres still ring in the ears of those of us whose ears are open.

FIG. 7.—JOHN C. WARREN.

As a consequence of such conditions, operations were rare in civil practice. Keen* has given some interesting figures: "It is a striking commentary on the immediate results of anesthesia to learn that in the five years before the introduction of ether (1846) only one hundred and eighty-four persons were willing to submit themselves to such a dreadful ordeal in the Massachusetts General Hospital—an average of thirty-seven operations per annum, or three per month. In the five years immediately succeeding its introduction, although the old horror could not at once be overcome, four hundred and eighty-seven operations, or almost one hundred annually, were performed in the same hospital. During 1898 in the same hospital * * * over 3700 operations were performed."

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* Keen: "Addresses and Other Papers," p. 287.

Anesthesia did not spring full-fledged from darkness. For years men sought it, and some thought they had found it. It was a shrewd American dentist, **W. T. G. Morton,** who established publicly the use of ether as a safe and sure anesthetic, in 1846. His first demonstration was made on October 16th of that year, at the Massachusetts General Hospital in Boston, and John Collins Warren, the senior surgeon, then in his sixty-ninth year, was the daring operator to sanction and utilize the experiment. For several years Morton had considered this question of anesthesia. He had seen nitrous oxid tried, and he had experimented with sundry substances. C. F. Jackson, the chemist, had encouraged him to employ sulphuric ether, which he did by tests upon animals, upon himself, and upon one other patient before making his public demonstration. The achievement was an admirable piece of scientific work, for which the man received scant reward. However, anesthesia was accomplished: the use of ether, and the next year of chloroform, became universal throughout the civilized world, and the science of medicine moved forward into the antiseptic era, which occupied the next generation. Though Warren did not *discover* ether anesthesia, the profession must not forget its debt of gratitude to him for courageously seconding the discoverer and risking his great reputation and his patient in an unexplored field. Warren died in 1856, having lived to see his son, J. Mason Warren, associated with himself as colleague at the Massachusetts General Hospital. After a successful career J. Mason Warren in turn was succeeded in the same hospital by his son.

Mott and Warren may be regarded as the last American exponents of the Hunterian era.

The middle American period is rich in conspicuous names and is notable for two events—the introduction of ether anesthesia and the surgery of the Civil War. Most of the men famous in this period were educated in Europe, because to Europe we still turned for the best original work in science and for the experience of great clinics. With the Napoleonic era the Paris school became conspicuous and popular. It was favored by the Government and unusual opportunities were offered there for the study of anatomy and clinical surgery. Less and less, as time went on, do we hear of Americans in Edinburgh and London; but the results of the Paris teaching were being felt, and we were developing rapidly a new generation of practitioners in America. Conspicuous among these were the Philadelphia group. There was **William Gibson** (1788–1868), born in Maryland, Professor of Surgery in the University of Maryland in 1812, and in the University of Pennsylvania from 1819 to 1855. He published his "Institutes and Practice of Surgery" in 1824, and the book went to the eighth edition. Gibson was the first to perform ligation of the common iliac (1812); and he operated twice upon the same patient by Cæsarian section.

John Rhea Barton, born in 1794, was surgeon to the Pennsylvania Hospital. He is known especially for his work upon bones and joints, and with his name is associated a form of fracture of the lower end of the radius, Barton's bandage for fracture of the jaw, and osteotomy for ankylosis of the knee, first performed by him in 1826. In 1834 he wired a fractured patella. He died in 1871.

George McClellan was born in 1796. He was a pupil of Dorsey, Physick's nephew, and was graduated from the University of Pennsylvania in 1819. McClellan will always be known as the founder of the Jefferson Medical College of Philadelphia in 1824, where he held the chair of surgery until 1838. He was a brilliant operator, bold and confident. He excised the lower jaw in 1823, and the parotid gland; and was one of the first to remove the entire scapula and clavicle for malignant tumor. The clavicle had previously been excised for necrosis, and for the first time, by McCreary of Kentucky, in 1813; while the entire scapula, three-fourths of the clavicle, and the arm were excised for the first time, and successfully, by Dixi Crosby of New Hampshire, in 1836. McClellan died in 1847 at the age of fifty-one.

Another distinguished Philadelphian was **George W. Norris** (1808–1875), a graduate of the University of Pennsylvania in 1830. He was surgeon to the Pennsylvania Hospital and Professor of Clinical Surgery in the University; and his valuable statistical contributions to practical surgery, published between 1828 and 1854, rank him among the best surgical writers of his day.

Thomas Mütter, born in 1811 in Virginia, was graduated from the University of Pennsylvania and became Professor of Surgery in the Jefferson Medical College. He is celebrated for his plastic operations for extensive scars. He died in 1859. The Mütter Lecture and the Mütter Museum of the College of Physicians of Philadelphia are notable foundations due to his generosity.

Daniel Brainard was born in Western New York in 1812, was graduated from the Jefferson Medical College in 1834, and settled in Chicago. He amputated at the hip-joint in 1838, but his most famous service was the founding of Rush Medical College of Chicago.

Other distinguished Philadelphians were **Joseph Pancoast** (1805–82), in 1838 elected Professor of Surgery in the Jefferson Medical College, a strong writer on surgery and distinguished for his plastic operations, resection of nerves, and his work on ununited fractures; **Henry H. Smith** (1815–90), Professor of Surgery in the University of Pennsylvania in 1855; **Francis Maury** (1840–79), the first in this country to perform gastrotomy; and **D. Hayes Agnew** (1818–92), who taught first in the Philadelphia School of Anatomy,* and later became Professor of Surgery in the University of Pennsylvania. He published "Principles and Practice of Surgery" and was for more than a generation a famous and highly esteemed practitioner and teacher.

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* This school was founded in 1820 and was a "School of the Prophets" in training future professors in many departments of medicine. It ceased to exist in 1875, having had a longer existence as an extramural teaching institution than any other such school except that of the Hunters in Great Windmill Street, London. A history of the school has recently been reprinted by W. W. Keen in a volume of "Addresses and other Papers."

In New York during this middle period were **J. Kearny Rogers** (1793–1851), an able surgeon of the New York Hospital, and **Willard Parker** (1800–84), a Harvard graduate and pupil of John C. Warren. Parker's was a remarkably successful and conspicuous career. He was a teacher in many schools, in Berkshire, Cincinnati, and the College of Physicians and Surgeons in New York. He was a surgeon to Bellevue and the New York Hospitals. Billings says that he was the first to operate for strabismus in this country. More than that, though he was not the first surgeon to operate for abscess resulting from appendicitis, his paper in 1867 was the first which compelled the profession to recognize the need for operation.

Bigelow is one of the notable names in American medicine. **Henry J. Bigelow,** of Boston (1816–90), was the son of a distinguished father, Jacob Bigelow. For more than fifty years the younger Bigelow was eminent. Appointed surgeon to the Massachusetts General Hospital in 1846, and Professor of Surgery at Harvard in 1849, he served with distinction until his retirement from the hospital in 1886. He was one of the best products of the French school—a brilliant, meteoric teacher, a profound and exhaustive writer, a bold operator. The story of his life is full of interest, but he is known to us today mainly for his explanation of hip-joint dislocations—he named the Y-ligament—and for his elaboration of litholapaxy.

Besides these more conspicuous exponents of American surgery, there were appearing here and there men who performed deeds, sporadic deeds, many of them, of which the student of our history should read. **Bobbs,** of Indianapolis, devised the operation which is known to us today as cholecystostomy. He operated first in 1867, thirty-nine years ago, and removed fifty gall-stones. The next year, 1868, **J. Marion Sims** (1813–83), of New York, operated in the same way and removed sixty stones from the gall-bladder. He also introduced the silver wire suture in operating for vesico-vaginal fistula, and was one of the pioneer gynecologists of America. In 1850 **Morrill Wyman** and **Henry I. Bowditch** performed the operation of paracentesis thoracis, a great improvement over the familiar old proceeding of Hippocrates. Glancing back nearly to the beginning of the century, we read of **Brashear,** the pioneer Kentucky surgeon, who first in this country successfully performed primary amputation at the hip-joint, a feat which was not repeated until Mott's operation in 1824. **Gurdon Buck,** of New York, followed Parker in operating for appendicitis; he devised his well-known apparatus also for thigh fractures, in 1851, and excised the olecranon in 1842; while **Carnochan,** in 1856, excised the second branch of the fifth cranial nerve beyond Meckel's ganglion, for the relief of tic, and in 1853 excised the whole of the ulna.

John L. Atlee (1799–1885) and his brother, **Washington L. Atlee** (1808–78), of Pennsylvania, **Dunlap, Peaslee, Kimball, J. Marion Sims,** and **John Homans** advanced and placed upon a sound basis the operation of ovariotomy.

Such are some of the prominent names which strike one in reviewing the American surgical literature of the middle of the century. The Civil War followed, when the services of these men and their ingenuity were turned to the succor and relief of those wounded in battle. Though the mortality was high, according to modern standards, the record is a brilliant one, and the immense literature of the medical and surgical history of the Civil War deserves careful study.

The last era with which we have to deal is the present era, and is concerned largely with living men. I have called it the German-American era, because it has been influenced enormously by the teachings of the German schools, whither the students of this generation have flocked in multitudes; but it depends also upon American accomplishments and upon work perfected in our own country by men whose initial training was largely German. One conspicuous man, in his day one of the most widely known surgeons in America, was **Samuel D. Gross** (1805–84). He belongs to the border-land between the French and the German-American eras. His work for surgical progress was so important, so far-reaching, and so thorough that he merits more than the brief mention we can give him here. Gross was a graduate of the Jefferson Medical College, and began his teaching life in Cincinnati and Louisville, after which he went to New York, and finally was called to the chair of surgery in the Jefferson

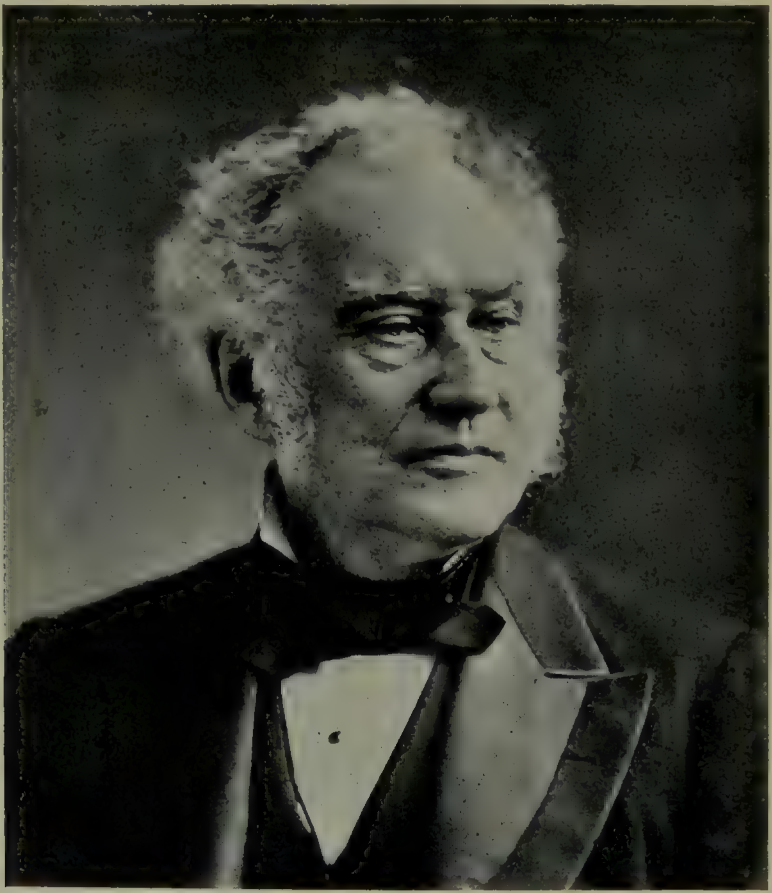

FIG. 8.—SAMUEL D. GROSS.

School, in 1865, which he held until he retired in 1882. He was a great teacher, a voluminous writer, and a man of the widest acquaintance. He and Bigelow caused American surgery to be respected in Europe, and he had the unique honor of being a laureate of Oxford, Cambridge, and Edinburgh. First of American authorities, he wrote a systematic treatise on pathologic anatomy. He was a publicist with many interests. He was a medical historian. Among his objects of special surgical importance was the investigation of abdominal stab wounds, the excision of the trifacial and spinal accessory nerves, the perfection of a urethrotome, and the study and treatment of tumors.

Samuel D. Gross is one of our few great surgeons who has been suitably honored by posterity. In 1897 the American Surgical Association, with the coöperation of the Alumni of Jefferson Medical College, erected in the city of Washington, to his memory, a handsome statue which stands in front of the Army Medical Museum.*

With this brief statement of what Americans have been doing, let us bring to a close, at the beginning of the present era, the story of their achievements. The present era is that which we properly call the era of modern surgery. It began with the introduction of antiseptic methods, and it has nourished and developed some of the greatest men in our surgical history. Many of these men are now living, their work not yet completed. They have contributed enormously to the advancement of our art in many fields. American accomplishment in abdominal surgery, in neurologic surgery, in genito-urinary surgery, in gynecology, and in the treatment of the eye, the ear, the throat, and the lungs, needs no apology. It stands for the best work being done in the world. Let us pass on to a consideration of the famous Englishman to whom our era owes the most, Joseph Lister.

JOSEPH LISTER.

Born 1827.

The nineteenth century is immediately behind us. That is a phenomenon we are not likely to forget if the writers shall have their way. Six years ago we began the present century by celebrating the achievements of the last century, and, truly, the more we inspect those hundred years of progress, the more remarkable they appear. The advances in surgery have been marvelous; to the superficial observer they appear miraculous. In 1894 Billings wrote:† "More progress in the art has been made since 1800 than had been made in the two thousand years preceding that date." In 1904 Dennis said: "Surgery as a science made no profound impression upon the world until about a century ago." Such statements are specious, and are true in a special sense only. The achievements of the last century are wonderful indeed, but I have written these pages to little purpose if I have failed to show that the foundations of our art as well as of our science were laid deep long before the beginning of the nineteenth century. Galen is a man to be reckoned with, and Vesalius, Paré, Harvey, and Malpighi, to say nothing of Haller and the Hunters. Such men were needed for the development of Cooper, Physick, Brodie, Warren, Syme, Paget, Dupuytren, Nélaton, Velpeau, Bigelow, von Graefe, von Langenbeck, Billroth, and Lister. The great and permanent achievement in surgery of the nineteenth century was the wide development and establishment of scientific methods of study. Out of those methods have come the marvels which we boast. Without them Morton would not have discovered anesthesia, nor Lister antisepsis; and Humphrey Davy, Jackson, and Pasteur were necessary to Morton and to Lister. History shall determine all this and shall correct our present perspectives.

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* "Trans. Amer. Surg. Assoc." 1897.

† Dennis's "System of Surgery," i, p. 91.

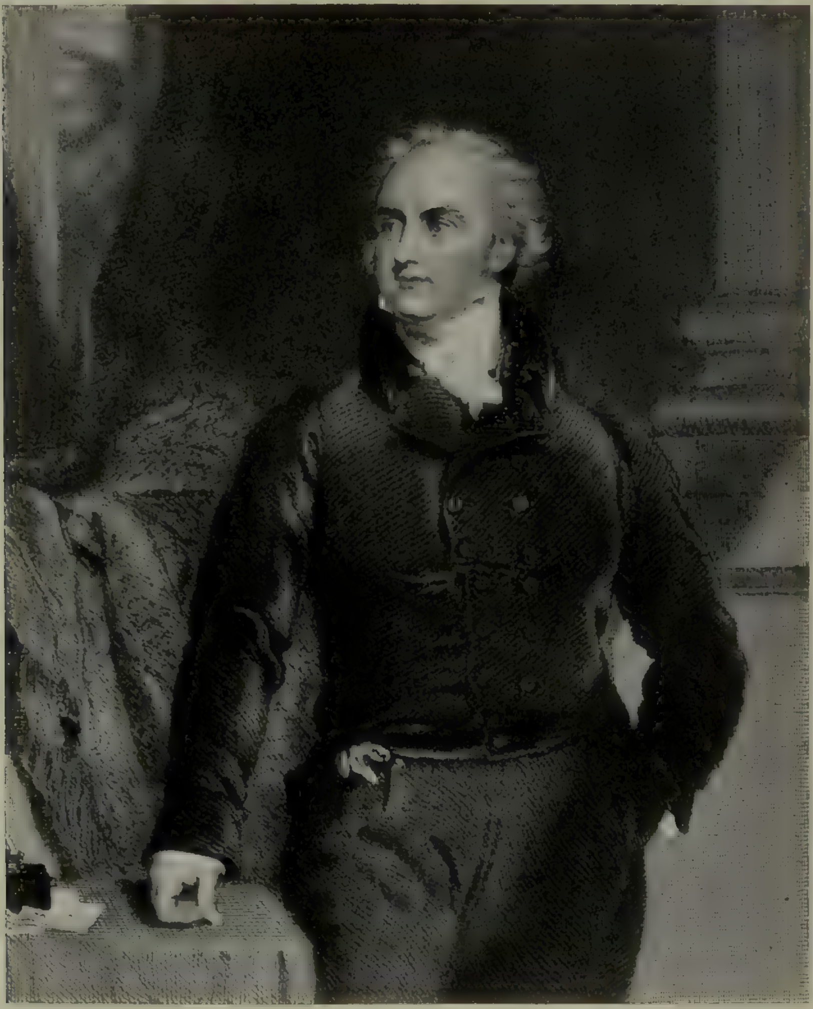

FIG. 9.—SIR ASTLEY PASTON COOPER, BART.

All men, today, will agree that Joseph Lister is the commanding figure in the surgery of the nineteenth century; and I shall attempt, in the few pages that are left, to tell something of that great man, to place him in his proper setting and to sum up his achievement. He is still living, but, if he should chance to read these lines, he needs not this evidence that nowhere more than in America is his name revered and his teaching followed.

Thirty-four years elapsed between the death of John Hunter and the birth of Joseph Lister—a brief interval as science reckons time; while between the date of Hunter's last publication and the time of Lister's first studies in the antiseptic treatment of wounds there was an interval of nearly seventy years. It is worth our while to inquire somewhat into the doings of the surgical world during those seventy years. Names attract us first, and there are great names. In Great Britain and in our own America Hunter's pupils and their pupils carried on his work. During the first quarter of the last century London and Edinburgh were the resorts of students from all countries. There was the brilliant **Astley Cooper** (1768–1841), whose charm of manner, wide learning, phenomenal skill, and enthusiasm for his profession made him the most popular teacher of his time; **John Abernethy** (1764–1831), Cooper's colleague and rival, thought by many to be more deeply imbued with Hunter's teachings than any of his contemporaries, an able successor and exponent of his master. There also were Cline, Blizard, Home, Lawrence, and Wardrop in the same group. All were sound investigators, teachers, and writers. **Benjamin Collins Brodie** (1783–1862) belonged to a somewhat younger generation. He was a brilliant anatomist and operator, but was noted chiefly as an exhaustless physiologist and a delightful writer. Then there were **Charles Bell** (1778–1842), of Edinburgh and London, whose fame rests mainly on his discovery of the functions of the two roots of the spinal nerves, and his researches into the anatomy of the brain and of expression; Philip Syng Physick (1768–1837), of Philadelphia, a favorite pupil of Hunter, and his prophet in America; and John Collins Warren (1778–1856), of Boston, the first surgeon publicly to employ ether anesthesia (1846). Coming down further into the century, there were **Robert Liston** (1794-1847), of Edinburgh and London, famous for his strength, daring, and weird feats in the amphitheatre; **James Syme** (1799–1870), a renowned teacher in Edinburgh, a copious writer on excision of joints, amputations, and surgical pathology, and author of a text-book of surgery. He was Lister's father-in-law and the surgeon in "Rab and His Friends." **Abraham Colles** (1773–1843), of Dublin, was the first to describe that fracture of the radius which goes by his name; **Fergusson** (1808–77) was for many years the leading operator in London; **Erichsen** (1818–90) was the author of one of the best-known text-books which educated thousands of English and American students; while **James Y. Simpson** (1811–1870) aided to make the Edinburgh school renowned by his researches in the domain of both surgery and obstetrics. He is best known to us for his introduction of chloroform as an anesthetic in 1847. **Sir James Paget,** through his "Lectures on Surgical Pathology" (1853), gave a new impetus to scientific studies left unfinished by John Hunter. Those are a few of the men who made famous Scotch and English surgery. They developed hospitals, reorganized schools, and worked out a masterly technic of the old style. With their limited means, they set a pace which the present generation may regard with profound admiration.

Meantime, on the Continent, new men rose to fame, new schools were established, new centers were developed, and great reputations were achieved. The political conditions which grew out of and succeeded the French Revolution produced strange combinations and brought to the front vigorous and fresh blood, which otherwise might have languished. The wars produced a great line of army surgeons; the problems of transportation, of field and hospital service, of operative measures, the combating of surgical infections, and the after-treatment of the wounded continually exercised ingenious minds. With enlarged political conditions native talent found encouragement, and monarchs came to see that genius of all sorts must be encouraged if nations are to compete successfully with their rivals. So one finds Napoleon drafting young men into his schools of military surgery, securing for them distinguished instructors, introducing rational anatomy laws, encouraging competition, and fostering science. Vienna, Berlin, and other capitals followed the lead of Paris; medical schools and their associated hospitals became part of the government system; medical education and the license to practise were made matters of vital concern to the State; great research laboratories were instituted, museums and libraries were collected, and facilities such as the world had never yet seen for medical education were provided and made imperative.

Great surgeons grew up under such a system, and their works were commensurate with their pains. At a few such men let us glance. The Paris school and hospitals were the most famous in the second quarter of the nineteenth century. The school, fostered by government, was definitely organized in 1804; in 1806 the Imperial University was created, and in 1808 the medical school became its faculty of medicine. **Dominique Jean Larrey** (1766–1842) was Napoleon's great army surgeon. You shall read with delight his "Memoirs of Military Medicine," a mine of information. He appreciated the value of surgical rest, and relates scores of remarkable and instructive cases. He lived for years as the beloved Nestor of the profession. **Guillaume Dupuytren** (1778–1835) was surgeon-in-chief to the Hôtel Dieu, from 1815. He was a bold, self-reliant, stern, unpopular man, a physiologist and pathologist, and for years a great power in the world of surgery. **Jacques Lisfranc** (1790–1847) is famous for his amputation of the foot; he was a past-master in all sorts of amputations and was known also for his excisions of the jaw, the rectum, and the cervix uteri. **Jean Civiale** (1792–1867) made his mark as a great genito-urinary surgeon. **Alfred Armand Louis Marie Velpeau** (1795–1867), surgeon to La Pitié and professor of clinical surgery in the faculty, after 1833, was a strong, resourceful, and useful man, a thorough anatomist and an able operator. He was a great worker and a splendid teacher—perhaps the most valuable surgical member of the French school in the first half of the last century.

Joseph Francois Malgaigne (1806–1865) is the greatest surgical critic and historian known to us. As a speaker and publicist he will endure, but his work as a practical surgeon is ephemeral. **Auguste Nélaton** (1807–1873) is thought by many to be the best surgeon who has yet appeared in France—diagnostician, operator, teacher. He published "Elements of Surgical Pathology" in five volumes.

So much for a few of that famous French school upon which one fain would linger. It is hard to pass by such names, but so, too, with a few Italians and many Germans. There was the great surgeon and anatomist, **Antonius Scarpa** (1752–1832), of Modena and Padua—he of Scarpa's triangle; **Vincenz Sebastian von Kern** (1760–1829), the great Viennese surgeon from 1805 to 1824; and **Philip Franz von Walther** (1782–1849), professor of surgery at Munich after 1830, the founder of modern surgery in Bavaria. **Carl Ferdinand von Graefe** (1787–1840) from 1810 was the distinguished first professor of surgery at the newly established University of Berlin. **Johann Friedrich Dieffenbach** (1792–1847) succeeded von Graefe at Berlin in 1840; a great and ingenious operating surgeon, he is known to us especially as the originator of the operation of tenotomy for strabismus. **Maxmilian Joseph von Chelius** (1794–1876) wrote a delightful and valuable "Handbook of Surgery," which had a wide influence. He was professor of surgery at Heidelberg.

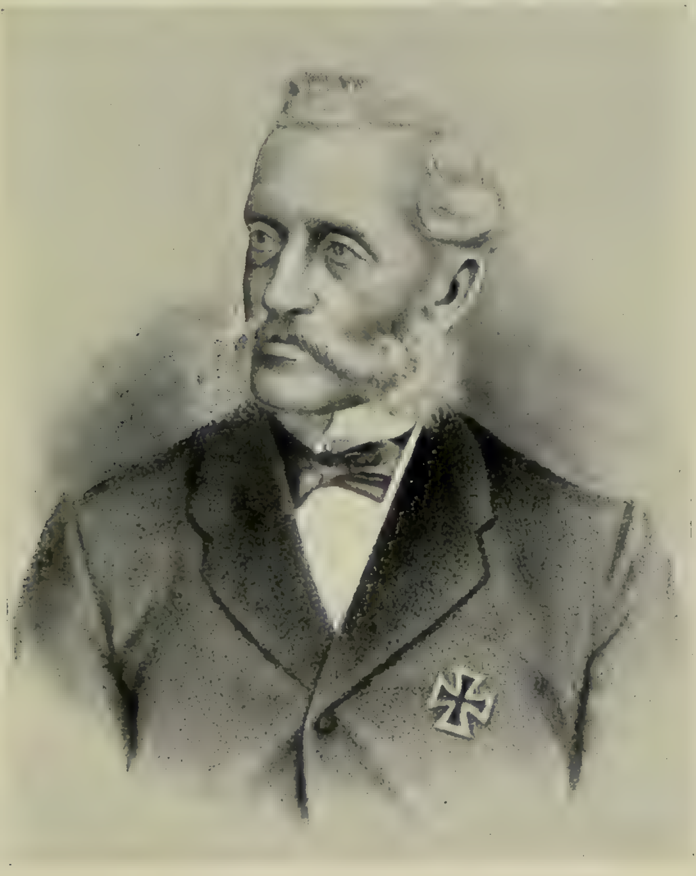

Fig. 10.—Bernhard R. K. von Langenbeck.

The most eminent German surgeon of the last century was **Bernhard Rudolph Konrad von Langenbeck** (1810–1887), the Astley Cooper of Germany. von Langenbeck succeeded Dieffenbach in the chair of surgery at Berlin in 1847, and for forty years was a power in the land. He devised numerous operations, made countless improvements in technic, and established two important journals of surgery; but, as Billings says, his greatest contribution to surgery has been his pupils. Passing over Zeis, Stilling, Heine, Loeffler, Lücke, Hueter, Maas, Vogt, Volkmann, we must recall especially **Theodor Billroth** (1829–1894), the famous professor of Vienna after 1867. He was a pupil of von Langenbeck and was almost equally remarkable. A many-sided man, interested in and concerned with every new thing, he was a daring and original operator and an inspiring teacher. He excised the larynx in 1873 and the stomach in 1881. Dozens of American surgeons, now active, studied under him, and his name is a household word among us.

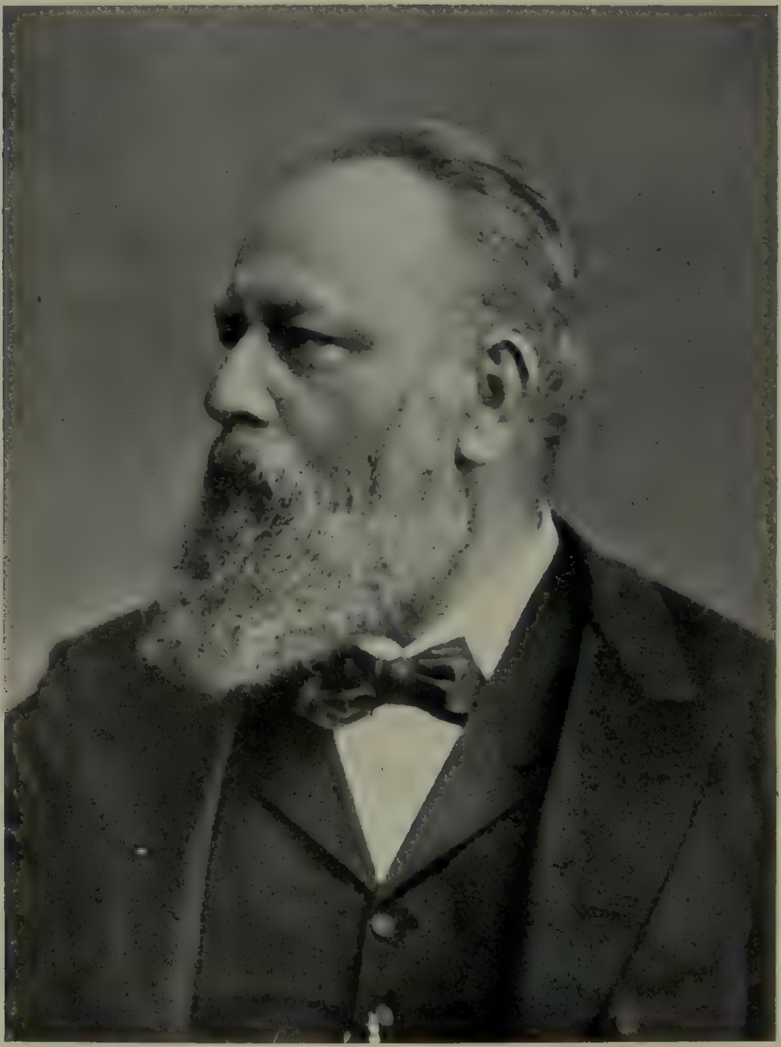

FIG. 11.—DR. THEODOR BILLROTH.

We have seen that the two great surgical events of the last century were the discovery of anesthesia and the development of antisepsis. In a measure the two go together. Either would be less effective lacking the other. Lister was a student in University College, London, when ether anesthesia was demonstrated in Boston; and though he had not yet begun his medical studies, the fame of the discovery, if not the enthusiasm for it of Liston, who, first of English surgeons, used ether in the North London Hospital, must have stirred Lister's youthful mind.

Joseph Lister was born on April 5, 1827, at Upton, in Essex County, England. He is not a Scotchman, as many think, though his notable work was done in Scotch universities. His biography has not yet been published, so that material for a sketch of Lister's career is scanty and scattered. Four years ago (1902) there was the Lister jubilee, to commemorate his fifty years of professional life. English medical journals celebrated the event in articles furnished by some of his old friends and pupils. From such sources and from the writings of the man himself one may construct a broken story. As the "British Medical Journal" says, its contributors "have related the biography of a scientific thesis rather than of the man who established it."

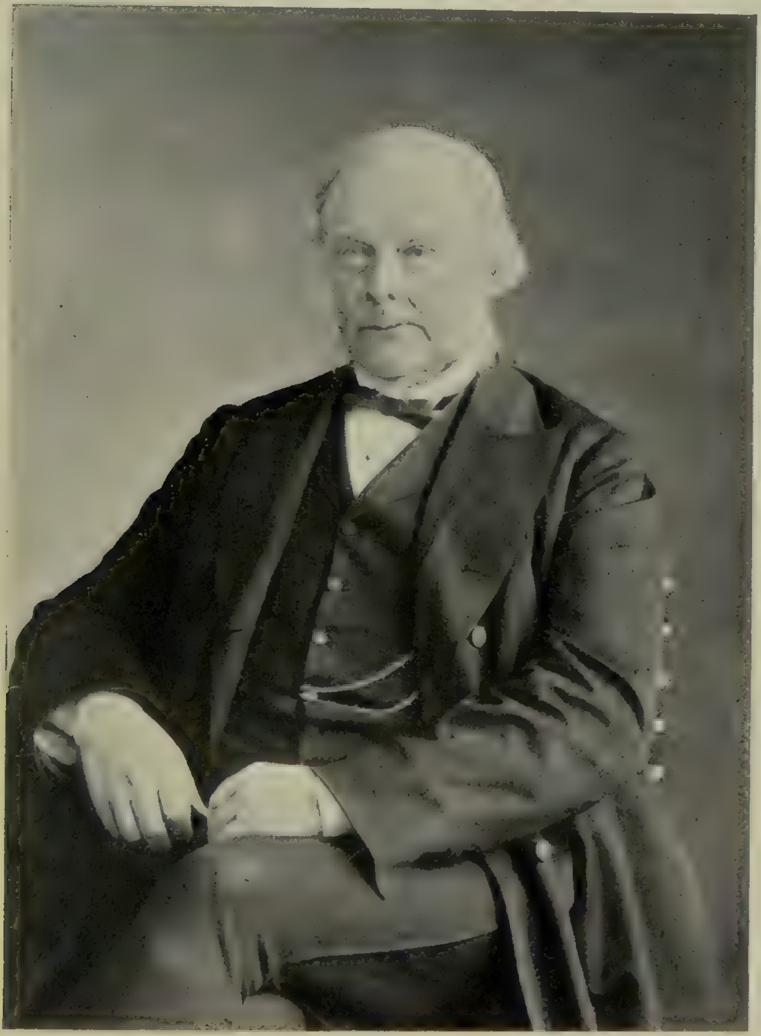

FIG. 12.—LORD LISTER, O.M., F.R.S., F.R.C.S.

Lister's father was Joseph Jackson Lister and his mother was Isabella, daughter of Anthony Harris, of Maryport, Cumberland. The elder Listers were Quakers. The mother died in 1864 and the father in 1869. Joseph Jackson Lister, following his own father's trade, was a wine merchant in London, but in spite of the claims of business, he was through life an earnest student of science. He made important improvements in the microscope, and in the year that saw the birth of his distinguished son, he published, with Thomas Hodgkin, a paper entitled "Some Microscopical Observations of the Blood and Animal Tissues." His son wrote a life of him for the "Dictionary of National Biography," from which it appears that the senior Lister was a useful and constant contributor to the construction of the microscope and to microscopic studies. In 1834 he became a Fellow of the Royal Society.

Joseph Lister was carefully educated for his profession. He went to a private school, as a lad, and then to University College, whence he was graduated B. A. in 1847. In that same year, at the age of twenty, he began the study of medicine, which he followed zealously for five years in the Medical Faculty of University College and at University College Hospital. During this course he was greatly influenced by Graham, professor of chemistry, and Sharpey, professor of physiology—strong and inspiring men. His father's influence with him was important, too, in those years, so that we hear of the young man's devoting himself early to histologic research. His first published paper, written in 1852, dealt with the existence in the iris of tissue identical with ordinary unstriped muscle, and with its distribution. In 1853 he produced "Observations on the Muscular Tissue of the Skin." Meantime, in 1852, he had been graduated M. B., and had become a member of the Royal College of Surgeons. In the hospital Lister served as dresser and house-surgeon to J. E. Erichsen; his own house-surgeon and senior while he was in the former office being Henry Thompson. Of those early years we know little as yet, though we must believe they were fruitful years; for what years of Lister's busy life have failed of accomplishment?

On leaving the hospital he followed the advice of Sharpey and Thompson, and went to Edinburgh. Sharpey told him to take six weeks of Syme's clinic. Now, Syme had gone up to London to be a surgeon to the University College Hospital in 1848, for a few months after Liston's death. So Lister went to Scotland for six weeks, and in Scotland he worked and taught for twenty-three years. He went to Scotland an obscure student; he returned to England one of the lights of the surgical world.

One may divide geographically the progress of Lister's career: A youthful period in Edinburgh, from 1854 to 1860; Professor of Surgery in Glasgow, from 1860 to 1869; Professor of Clinical Surgery in Edinburgh, from 1869 to 1877; Professor of Clinical Surgery in King's College, London, from 1877 to 1893, when at the age of sixty-six he retired from active teaching and was made Emeritus Professor of Clinical Surgery and Consulting Surgeon to the Hospital.

At the time of Lister's going to Edinburgh the frightful mortality of troops in the Crimean War was exercising men. Soldiers were being killed in battle by tens and hundreds, but they were dying of surgical diseases by thousands. The newly aroused science of Europe was keenly aware of these facts, and in the great hospitals surgeons groped after causes and remedies, fruitlessly for the most part. Indeed, a sort of fatalism appeared to be settling upon the profession. That hopeless view seems never to have subdued Lister. Sir Hector C. Cameron writes that "the grief and mental worry arising from such experiences, often repeated, produced in Lister's mind a sense of discontent with things as they were, and this seemed to many of us who were his pupils in strange contrast to the resignation with which some of his colleagues viewed similar experiences."

One cannot say just when it was that Lister began constantly turning his mind to the problem of a remedy for wound infection. Perhaps he himself could not tell us now, but he must have been dwelling upon such things very early in his career. We may conceive of the condition in those old hospitals, and of wounds in general, from the descriptions in the books and from the tales of men whose professional memories go back thirty-five years or more. In the hospitals surgical sepsis ran rampant. Secondary hemorrhage, erysipelas, septicemia, pyemia, and "hospital gangrene" were endemic. Sometimes wards, wings, or whole institutions were closed, in vain attempts to stamp out these disorders. Operations in private houses, especially in the country, were less dangerous than in hospitals, but even in private practice the mortality from sepsis was high. Sometimes a surgeon would wear the same old operating coat for years, and would pick waxed ligatures from the button-hole of his assistant, who carried them there for the convenience of his chief. Old hands will tell you such stories by the score. To the modern surgeon it is a barbarous era.

In Edinburgh Lister acted for a time as resident surgeon to Syme at the Royal Infirmary, and in 1856 became assistant surgeon to the same distinguished man. Syme was a brilliant and resourceful operator, and the admiration and affection between the two men was constant and abiding. Lister married Syme's daughter. Annandale tells how in the early days Syme often spoke to him of his appreciation of and pride in Lister's original scientific spirit and work, and his belief that such work would result in an important advancement of surgical practice. So far as one may judge, Lister has won through life golden opinions from those with whom he has come in contact. In his early days his colleagues admired him and his pupils accepted him with whole-hearted enthusiasm, even while the outside world heard him with a shrug or opposed him with vigorous incredulity. Lister's temperament and method were very different from those of John Hunter. He was never contemptuous, loud, or bellicose, but out of thorough study and careful observation drew conclusions which he put persuasively and persistently before the surgical world. The surgical world was forced reluctantly to accept them.

While in Edinburgh, besides assisting Syme, Lister gave admirable courses of systematic lectures on surgery, and carried out numerous original investigations, notably on the coagulation of the blood. One must remember that he is a practical surgeon as well as a laboratory student; in his active days he was an ingenious and able operator, as became the pupil of Syme, and for the greater part of his life he has been a professor of clinical surgery. He remained in Edinburgh in this early time until 1860, his thirty-fourth year, and it was during the last of this period that he began his bacteriologic studies in connection with antiseptic surgery. With an eye single to this great problem he kept a lookout for what the rest of the world was doing, and it was now that the significant researches of Pasteur attracted him. It is well for us, too, to take note of the great Frenchman and of his service to surgery.

Louis Pasteur was five years Lister's senior. The son of an old Peninsular veteran, he was well educated for a scientific career, and was a pupil of Dumas, the famous chemist.* The story of his studies in fermentation and spontaneous generation is a classic of scientific literature. By 1860 he had convinced himself of the importance of the rôle played by microbes in the production of fermentation, as opposed to the old view of Liebig, that it is a "change in organic fluids and tissues set in motion by the access of oxygen or of bodies in a state of decomposition." After the demonstration of the cause of fermentation, there followed experiments and discussions on spontaneous generation and the establishment of Pasteur's thesis of the non-existence of such generation.

These two great facts being admitted, what was their bearing upon putrefaction and wound infection? Vallery-Radot tells an anecdote of Pasteur's interview with Napoleon III in 1863, when the Emperor questioned Pasteur closely on his studies and conclusions. The next day Pasteur wrote: "I assured the Emperor that all my ambition was to arrive at the knowledge of the causes of putrid and contagious diseases."

This is not a history of bacteriology, but we are dangerously near that fascinating topic. Suffice it to say that in Scotland Lister's growing belief in an external agent as the cause of wound infections was strengthened and confirmed by Pasteur's researches, for in 1867 he was able to write: "Turning now to the question how the atmosphere produces decomposition of organic substances, we find that a flood of light has been thrown upon this most important subject by the philosophic researches of M. Pasteur, who has demonstrated by thoroughly convincing evidence that it is not to its oxygen or to any of its gaseous constituents that the air owes this property, but to minute particles suspended in it."

In 1860 Lister had achieved so enviable a reputation in Edinburgh as a brilliant and sound teacher and judicious operating surgeon that he was called to the professorship of surgery in the University of Glasgow. The next year he was made a surgeon to the Royal Infirmary there. In both offices he met with gratifying success, and, as one would expect, he continued to devote himself, in this broader field, to the problem of antiseptics. He believed then and for many years afterward that the air was the vehicle which brought poison to wounds, though he recognized then and with increasing perception as the years passed that all foreign substances—clothing, skin, instruments, sponges, ligatures—were also contagion-carriers. Even before finding a satisfactory antiseptic he insisted that operators and dressers should be scrupulously clean, and he employed sundry deodorant lotions about wounds. He had not then concluded that putrefaction and suppuration are distinct processes and are due to distinct causes. He regarded wound-infection as putrefaction; and what wonder, considering that putrefaction did frequently occur and simulated inflammations of the most virulent type? The science of bacteriology was in its infancy, and no one appreciated the different forms of organisms, much less the distinction between pathogenic, pyogenic, and saprophytic bacteria.

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* Read Vallery-Radot's "Life of Pasteur," one of the most delightful and stimulating of biographies.

Whatever the active and offending agents might be, Pasteur's teaching confirmed Lister's opinion that they were omnipresent, and he sought an antidote. So he was led to his famous carbolic acid,* an agent little known then in Great Britain. He had been impressed by the action of carbolic acid employed in disinfecting the sewage of the town of Carlisle, where it had deodorized pastures and destroyed parasites which were said to infect cattle.

At that time Lister's ingenuity was exercised especially to save cases of compound fracture, in which the mortality had always been great, and it was in such cases, in 1864, that he proposed to use his new remedy. He recognized that the most severely lacerating *simple* fractures healed without special disturbance, and convinced as he was that it was the air admitted to *compound* fractures which rendered them dangerous, he sought to reduce them to the *simple* state by excluding air, or by opposing to the air a barrier which should render harmless its offending germs. Accordingly he wiped out the wound with pure carbolic acid and then sealed it with lint soaked in carbolic. The exudations, mingling with the acid, formed a paste which soon hardened into a firm scab. In order to prevent too rapid evaporation of the agent he laid over this dressing a block-tin shield. So long as active inflammation did not appear, the carbolic scab was painted daily with more carbolic to keep in force a fresh supply of the germicide, and the shield was reapplied daily. The surprising success of this treatment in the case of compound fractures led to its employment in abscesses and in fresh wounds. Sometimes it was impossible to secure exudate of proper quality to mix with the carbolic for a paste, so an artificial paste of linseed oil, carbonate of lime, and carbolic acid was devised. This was Lister's famous "antiseptic putty."

In such fashion the work progressed during those nine Glasgow years. The antiseptic principle was gradually extended to all varieties of surgical lesions, to septic processes, to fresh accidental wounds, and to operation wounds—amputations, excisions, and their like. As yet the treatment was crude, and consisted merely in modifying and extending the carbolic acid applications. Says Cameron: "It only remains to be added that the effects of the new treatment upon the wards were in the highest degree beneficial, converting them from some of the most unhealthy in the kingdom into models of healthiness."

Syme retired from the chair of clinical surgery at Edinburgh in 1869, and Lister was called from Glasgow to take the vacant place. By this time the new treatment had been well advertised through the lectures, papers, and addresses of its author, and the world was beginning to listen, but with an indulgent smile. As Chiene says: "Lister devoted his introductory (Edinburgh) lecture to 'an endeavor to convince' his hearers of 'the truth of the germ theory of putrefaction,' 'the basis of a new method of treatment,' 'the antiseptic system.' "* These views were new to most of his listeners, and were heard with many questionings, but he continued to expound, to practise, and to demonstrate so effectively that when he left Edinburgh, eight years later, his theories had been received there and his precepts were followed in some fashion.

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* Küchenmeister, of Dresden, had reported good results from carbolic acid in 1860, and Lemaire's work on carbolic acid (which was then known as "acide phénique") was published in 1865.

Lister's second residence in Edinburgh marks a service of continued development. Pasteur and himself, as well as other students, were advancing along lines which meant a constant expansion of bacteriology and the intelligent application of its principles to the problem of sepsis and wound healing. The Franco-Prussian war of 1870 had its lessons for French and German surgeons; scourges raged through the armies, though such men as Volkmann, von Esmarch, and others were beginning to employ simplified measures and a more rational therapeutics. The voice of Lister was finding its echo even on the battle-field. At home the modest great man was gaining strength continually. A writer in the "British Medical Journal" tells of the feeling akin to awe with which the younger medical generation of those days saw Lister, in defiance of tradition and authority, but secure in the certainty of scientific truth, do many things which at that time were condemned by professional opinion as most dangerous procedures.†

In 1877 Lister made his final move to London, where he was called to the chair of clinical surgery in King's College. He went reluctantly, for he was fifty years old and had long been doing congenial tasks among friends; but the new field was wide, the audience great, and the urging strong.

We may not follow the detail of his subsequent career or the growth of his work. Suffice it that time brought important modifications in his practice but not in his theory. Particular antiseptics came and went, the carbolic spray was used and was banished. Air was found to be not a dreaded enemy and carrier of disease, but a kindly friend when properly entreated; surgical cleanliness, a germ-free environment, became recognized as the one thing needed. Heat, soap and water, the nail-brush, alcohol, and a few simple chemicals took their place in our armamentarium, and *asepsis* supplanted *antisepsis*. But the great underlying truth remained: that wound-infection comes from without the wound, that it flourishes under appropriate conditions, that it may be eliminated by appropriate measures.

Twenty-five years ago Lister had won his victory, and saw his principles adopted throughout the surgical world. Who may tell the effect of that victory on surgical progress? No man has reckoned the immeasurable saving of life, the incomputable relief of suffering, the opening of new surgical fields. Daring has become conservatism; rashness has become common sense. The cranial cavity, the thorax, the abdomen, the lungs, the heart, the intestines, joints, the ear, the eye, regions and organs which were once sacred to the action of disease, which were inspected on the post-mortem table only, are now opened freely to the renovating measures of the surgeon and to the gaze of every medical student.

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* In his Liverpool address before the British Association, 1896, Lister told simply the story of modern surgery and of his part in it.

† "Brit. Medical Journal," vol. for 1902, p. 1856.

Eloquent volumes have been written to celebrate these great themes; this feeble pen can but trace its eulogy in humble echo.

Lister, the man and scientist, has been rewarded in a manner, so far as our human rewards may express gratitude. The list of his honors and degrees would fill more than one of these pages. He is a member of all sorts of learned bodies at home and abroad; Oxford, Edinburgh, Dublin, Glasgow, Cambridge, Toronto, have loaded him with their highest diplomas; portraits of him hang in distinguished halls where they fix the eyes of the world's great ones; he has presided over august assemblies; Queen Victoria made him a baronet in 1883, and in 1897 he was raised to the peerage, with the title Baron Lister—the first and only representative of the medical profession to be so honored in Great Britain.

How shall one sum up and estimate what he represents? Writers are wont to describe surgeons as great for their knowledge, their multitude of patients, their writing of books, their popularity as teachers. A lower estimate is to count him the great surgeon who is a great handicraftsman. But who shall be numbered with the immortals? We know that mere mechanical facility in surgery is not enough. It is permanent contribution to knowledge which counts. The uninformed look to closet students for such contributions, but have we not seen great operators who were great contributors? Mere operators are not known to history. Even the typical clinical surgeon, Paré, is memorable to most men for his invention of the ligature only. In our own time and in America the question of the appendix has agitated men. Surgeons have reported their hundreds of appendectomies amid the winding of horns and screams from the gallery gods, but the prize lies with that modest scientist* who, twenty years ago, gave to the world a single paper, in which he described the significance of the appendix and its rôle in disease. Last year only was he rewarded with the LL.D. by his alma mater.

And so with Lister; thoroughly educated to use the tools of his trade, profoundly versed in the science of his time, he spent his youth in acquiring and perfecting himself in what the world already knew of surgery. In his prime a skilful operator because operating was part of his business, an accomplished clinician because clinical surgery was his forte, he appreciated that the greatest work in science is creative work. His genius grasped at a breathless possibility, never before conceived by conservative minds; and so, following those sound inductive methods known to science through the ages, he launched us upon an era which is truly the most brilliant in the history of surgery.

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* Reginald Heber Fitz.

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Most of the portraits in this chapter were kindly furnished by the Library of the College of Physicians of Philadelphia; that of Warren by his son, Dr. J. Collins Warren; that of Gross by his son, A. Haller Gross, Esq.; and that of Lord Lister by himself, through J. Bland-Sutton, Esq.

CHAPTER II.

SURGICAL PHYSIOLOGY.

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In the limited space set apart for this subject but few of the topics deserving attention will be considered, and these only in brief.

Definition.—The scope and the application of surgical physiology are similar to those of surgical anatomy and surgical pathology. It embraces such laws and factors as are used in surgical practice, which rest largely upon altered physiologic actions. There is scarcely a diagnosis made or an operation performed that does not draw heavily upon our store of physiologic knowledge.

SURGICAL PHYSIOLOGY OF THE CIRCULATION.

Heart.—As a muscle the heart is probably the most highly organized and performs the most important function of the various muscles—striped, non-striped, and mixed—of the body. It has a wider range of compensation and certain other characteristics and limitations that are of great importance surgically. In its response to trauma of various kinds it shows marked individuality. A stab or gunshot wound in one instance may cause only temporary alteration of function, while in another immediate death may result. Direct manipulation of the heart in one instance may have but slight effect, in others inhibition and irregularity at once appear. The so-called short-rib or solar plexus blow may cause instant death by mechanical inhibition of the heart (Fig. 13). Experimental research has definitely proved that the collapse or death thus caused is in no way connected with the solar plexus, the diaphragm, or the splanchnic nerves. From a therapeutic standpoint, no drug has as yet been found that will protect the heart against the important alterations as a result of mechanical manipulation or trauma. Neither are these phenomena modified by anesthetics. In operations upon and about the heart, then, prevention is the best treatment.

Physiologic research and clinical experience have shown that when the heart-muscle is damaged or its nutrition impaired by acute infection, by anemia, by arteriosclerosis or advanced age, by valvular lesions, by fatty degeneration or by overwork, as occurs in athletics, it is more susceptible to trauma and mechanical interference than is the normal organ. One would hesitate much more to perform an operation on a senile heart than upon that of a young adult.

Acute dilatation and *paralysis of the heart* is a phase of surgical physiology that demands special attention. It is established that the output of the heart is dependent upon the blood-pressure in the large venous trunks and not directly upon the arterial pressure. When the amount of fluid entering the heart is increased, its work is increased in a geometric ratio; that is to say, if the amount of fluid is trebled, the amount of work is nine times greater—not three times. This fact, coupled with the fact that the heart is functionally impaired immediately on the diminution of its own blood-supply through the coronary artery, constitutes the most important group of physiologic factors as relates to the heart in the operative part of surgical practice.

In acute hemorrhage when the heart-muscle itself is functionally impaired by the diminished flow of blood through the coronary artery, if the amount of fluid is suddenly increased by a rapid intravenous infusion the heart's work is so rapidly increased in the presence of weakness that it may suddenly suffer an acute dilatation and an immediate paralysis, ending in death. In precisely another way acute dilatation may be produced and immediate paralysis and death be caused. If the intrapulmonary pressure is rapidly increased, as in certain methods of positive ventilation of the lungs in artificial respiration, the right heart may be unable to empty itself; the blood would then rapidly accumulate in the right side, causing a doubling, trebling, or quadrupling of its work in a moment. This would cause a lowering of the nutrition of the cardiac muscle, diminishes its power, and might cause an immediate fatal paralysis (Fig. 14). When these states arise either by an increased amount of fluid, as by an unwise intravenous infusion, or by obstruction of the pulmonary circulation or otherwise, the removal of the cause is the first consideration. The patient should at once be put in the feet-down inclined posture. In this position the blood will gravitate from the heart and the large thoracic veins into the splanchnic area and the large venous trunks in the lower extremities, thereby partially relieving the over-distention of the vessels. Following this, rapid massage of the heart by rhythmic pressure upon the thorax over it should be done, and artificial respiration maintained. In addition,

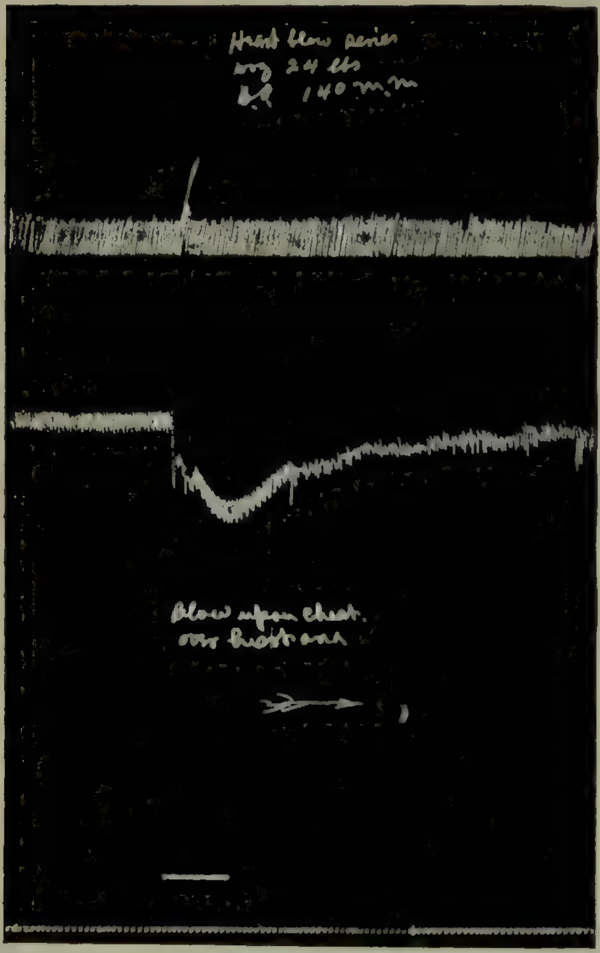

Fig. 13.—Blow upon the Chest Over the Heart.

Note the abrupt fall in the blood-pressure (second tracing) and the irregular heart-action later.

if it can be done quickly enough, extensive venous blood-letting from the jugular vein may be effective. From both the experimental and the clinical standpoints the efficacy of these measures has been well established.

In one of my own cases in the midst of an operation such a crisis arose, and acute dilatation was at once recognized by the extensive venous congestion, lividity, and simultaneous collapse of the pulse. It was during an operation on the neck. The jugular vein was in the field and was at once opened, and there was a gush of venous blood. During the same time vigorous massage of the heart was carried out by compression of the thorax, and the heart, which had stopped in paralysis, within a few minutes again beat regularly. The operation was completed and the patient recovered.

In certain anesthesia-accidents, as shown by Leonard Hill, the heart-muscle being impaired by the anesthetic may become acutely dilated and paralyzed. In such a case life may be saved by the plan of treatment just described. In such acute dilatation in anesthesia it is imperative that the patient either be bled or be put in the upright posture for a moment, followed by cardiac massage and artificial respiration, in order to resuscitate the heart.

The traditions of surgery have so long regarded cerebral anemia as the one condition to treat that the rational management of the heart has not received the attention its importance deserves. The differential diagnosis between collapse of cerebral origin and collapse of acute dilatation of the heart must be prompt and accurate, as the best treatment for one is the worst treatment for the other.

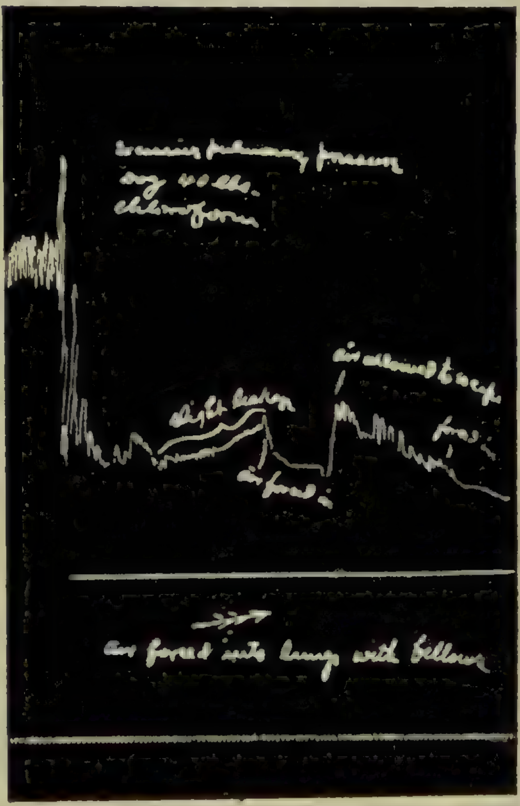

Fig. 14.—Positive Inflation of the Lungs Increasing the Trachea-Pulmonary Pressure by Means of a Bellows.

Note the momentary rise in the pressure, followed by an immediate staggering fall. The lower line indicates seconds.

In operations upon the thorax one must bear in mind the powerful influence respirations have upon the circulation. This will be discussed under another heading. Then, too, in certain operations upon the thorax in which respiration, and hence the supply of oxygen, is interfered with, it is well to take every precaution to see that the heart has its normal quota of oxygen to meet the various circulatory crises that the great disturbance of the circulation in thoracic operations so often entails. It is extremely important in every operation and in every anesthesia to take as accurate physiologic stock as possible of the cardiac reserve force. If there is an acute dilatation, a senile heart, a fatty heart, an anemic heart, the margin for safe operative disturbance is proportionately diminished and one must be prepared for sudden impairment or collapse unless its physiologic status is so accurately determined and the operative effect so perfectly controlled that the demand upon the heart falls within its physiologic margin of safety.

It is well, also, to bear in mind that what disturbs the heart most is the sudden changes in the blood-pressure or the sudden application of trauma or mechanical manipulation. Then, too, it is well to remember that the heart endures manipulation and trauma of its apex and the ventricles much better than of its base, including the auricles and the large venous trunks. If possible an operative procedure directed against the heart should be gradually approached, allowing time for the compensation and physiologic recovery from a slight manipulation, and should then gradually become more extensive as the heart recovers, until the ultimate aim has been reached.

When approached with due physiologic regard the heart is capable of withstanding a surprising amount of trauma and manipulation. In the event of collapse with sudden cessation of its beat, the heart may respond after a quiescence of a very considerable time—fifteen minutes or more. It is during these crises that one is apt to fall into the error of administering an overdose of saline infusion. In the senile heart, in certain lesions of the myocardium, in atheroma, in threatened breaks in compensation, and perhaps other cardiac states causing impaired action, a preliminary treatment with digitalis or strophanthus, or strophanthus with or without nitroglycerin may effectively improve the heart and thus increase the margin of physiologic safety.

Vasomotor System.—The surgical physiology of the vasomotor system is of such great importance to the surgeon that its consideration is worthy of a more detailed study than space will here permit. The height of the blood-pressure is due primarily to the action of the vasomotor center, which sends its nerve impulses through the vasomotor nerves to the vascular periphery. The rise and fall in the blood-pressure depends mainly upon the increase or decrease of the action of the vasomotor center. Roughly speaking, we may say that the heart energizes the blood-stream, supplying a sufficient amount of force to drive the blood through the smaller vessels known as the peripheral resistance area, making it return again to the heart.

While cessation of the heart's action means immediate death, it is no less true that the cessation of the activity of the vasomotor center causes death quite as certainly, though not so instantaneously. It is highly probable that from the vasomotor center more often than from the heart arise the causes of surgical death. Among these causes may be mentioned the paralysis of the center from operative or accidental trauma—usually designated shock—as a common example. In many of the infections the breakdown of the vasomotor center is perhaps the dominating factor in the causation of death. It is true that in the majority of instances life is terminated by the combined effect of a number of factors, such as the vasomotor, the cardiac, renal, respiratory, etc. In acute hemorrhage the vasomotor center is depressed on account of the lowered blood-pressure, which diminishes its supply of nutrition and of oxygen. The short pulse-wave is indicative of the relaxation of the vessels, which in turn is caused by a diminished action of the vasomotor center. That the low blood-pressure and pulse-characteristics are at least in part due to diminished activity of the vasomotor center is shown by the observation that when in this state, if adrenalin be given the blood-pressure at once rises and the pulse-wave is lengthened.

In asphyxia of any grade the vasomotor center is stimulated, producing a higher blood-pressure and a longer wave, and clinically it is characterized by a slow, full pulse. This slow, full pulse is often deceptive, giving a sense of false security. It is then true that what sometimes seems to be a marked improvement in the pulse is, when properly interpreted, a grave symptom.

The vasomotor system is the principal means of compensation in all the various crises occurring in the normal and in the pathologic state. When the blood-pressure is falling in one territory of the circulation an increased vasomotor action in another may compensate; if the area of the skin is dilated, the contraction of the splanchnic region may compensate and vice versa.

The splanchnic area and the brain have a certain and most important interrelation. To this subject Cushing has recently made important contributions. When the intracranial tension is increased, threatening to cause anemia of the vasomotor center, this center sends out strong impulses to the splanchnic area, causing extensive vascular contractions here, which in turn produce a marked rise in the blood-pressure, thus reëstablishing the amount of circulation of the vasomotor and other centers required for their normal function. In increased intracranial pressure from hemorrhage, from abscess, from depressed bone, from tumors, and other causes, unless other factors interfere the general blood-pressure usually is increased. The blood-pressure, which normally is, roughly speaking, from 120 to 135 mm., has been raised in pathologic intracranial pressure to 425 mm. mercury.

It will be seen, then, that the action of the vasomotor center in certain of the common forms of brain injury and disease becomes one of the strongest diagnostic features. We may say that a bounding pulse indicates an increased action of the vasomotor centers; a soft pulse, a diminished action. Recent studies have shown that the vasomotor centers are almost specifically affected in certain infectious diseases. Among those that interest the surgeon may be mentioned the various infections caused by pyogenic organisms. In most cases of acute infection the blood-pressure is raised because the vasomotor centers are stimulated. While this observation is as old as the literature of surgery, it is quite possible that we may now make some new applications in surgical diagnosis and prognosis.

In certain other acute diseases the toxic products depress the vasomotor centers. This is notably true in typhoid fever. In the course of typhoid fever an acute pyogenic infection may, on account of perforation of the bowel, or rupture of an abscess, be introduced. The circulation will then be subjected to antagonistic factors—the one tending to lower the blood-pressure, the other to raise it; but since the depressed vasomotor action due to the typhoid is the standard up to the time of pyogenic infection, one should expect a rise after such infection. This has been noted. In a number of observations in the acute infections, such as peritonitis, the blood-pressure is almost uniformly high in the early stages, the mean in adults probably being 150 to 160 mm., while in typhoid observations made on 150 cases it is shown to be, on the average, in the first week 104 mm., the third week 98 mm.

In typhoid the pulse is of large volume, in peritonitis it is small; in typhoid the pulse is soft, in peritonitis, hard; in typhoid it is slow, in peritonitis it is rapid; in typhoid dicrotism is usually present, in peritonitis rarely or never; in typhoid the wave is long, in peritonitis short; in typhoid the capillary pulse is frequently present, in peritonitis rarely or never; in typhoid there is usually an increased blood-supply—frequently not well oxidized—to the face, the front and the sides of the neck, and the upper part of the thorax, giving an almost characteristic dusky hue; in peritonitis there is a diminished supply of blood to this territory, giving an almost characteristic pallor.

The principal cause of the antithesis in these two important diseases is the characteristic effect of the several toxins upon the vasomotor center. Among the other evidences of typhoid perforation, then, the appearance of these physiologic alterations may be of very great assistance in the diagnosis. Drs. Cook and Briggs at the Johns Hopkins Hospital have made a very important contribution to this subject, their results being similar to those here given.

In our own experience in six cases of peritonitis following typhoid perforation, a rise varying from 8 to 40 mm. of mercury was noted. In three of these cases the first observations were made late; in two, early. The rise in the blood-pressure seems to occur very soon after the perforation. In other cases the picture was not so clear.

In a typhoid ward where blood-pressure records are carefully made as a routine, sudden alterations may be of extreme importance in assisting the diagnosis. It must be noted here, however, that the vascular system may be overwhelmed by the dosage of toxins in an acute infection and immediate collapse follow; furthermore, the shock due to the irritating effect of the toxins upon the peritoneum may also be a factor. This, if marked and if other factors can be excluded, may be quite as important as an increased rise in pressure. The very important topic of the surgical physiology of injuries and operations will be considered more fully under the chapter on Shock and Collapse.

RESPIRATION.

There are many phases of the surgical physiology of respiration that should be discussed, but we shall introduce here only a few of the most common. The diaphragm is the most important and probably the most typical muscle of respiration. The majority of the muscles of the shoulder girdle and neck with thoracic attachments, and classified as accessory muscles, have other functions to perform. This is true also of the abdominal muscles having attachments to the thorax. When the respiratory center is being gradually overcome by such anesthetics as chloroform and ether, the muscles of the neck and shoulder girdle, being more distinctly voluntary, are entirely paralyzed, after which the abdominal muscles and finally the diaphragm cease their function. This simple observation is of very great importance in anesthetics. The paralysis of the accessory muscles is a warning of excessive anesthesia which must be heeded. The diaphragm alone is entirely competent to supply the required amount of oxygen. This is shown in cases of high-fracture dislocations of the cord, in which all the accessory muscles are paralyzed. Were there occasion for an increased supply of oxygen, as in muscular exercise, the diaphragm alone would probably be incompetent. If a patient is depending entirely upon the diaphragm and at the same time pneumonia or pleurisy with effusion develops, or if there is distention of the abdomen causing interference with its free action, the diaphragm becomes incompetent.

The respirations are modified by numerous peripheral impulses. Sometimes one phase, sometimes another, is preëminently modified. In operations upon the pelvis in which contact with the sigmoid or rectum occurs, a prolonged, noisy inspiratory phase usually follows. The same is true of divulsion of the sphincter ani. Cold markedly stimulates the inspiratory phase. On the other hand, in operations upon the upper abdominal area in the neighborhood of the diaphragm, such as the search for gall-stones, the delivery of tumors, etc., the expiratory phase, usually noisy, is produced. General contact with the peritoneum causes an increase in the expiratory phase amounting sometimes to an expulsive action. This is particularly noted when intestines are being searched for gunshot wounds, and perhaps if haste leads one to employ undue force in returning them to the abdominal cavity, by which a marked expiratory and even expulsive action is produced. This requires increased manipulation on the part of the operator, which in turn causes an increased expiratory expulsive action. Thus a physiologic vicious circle is unwittingly instituted. In such an event, by a moment's rest with gentlest manipulation, the return of the intestines may be made so easily that it seems spontaneous.

Manipulation of almost any portion of the peritoneum causes an increased exchange of air. During this time the anesthetizer should be on the alert and should at least partially withdraw the anesthetic. This is particularly true when chloroform is used. Dangerous collapse and even death have been produced in this manner.

Manipulation of nerve-trunks and undue trauma in most parts of the body cause an increased respiratory action and must be reckoned with by the anesthetizer and the operator. The respiratory inhibitions are numerous and sometimes of great consequence. It has been well established that in the area supplied by the superior laryngeal nerves such inhibitions are prone to occur. The region of the epiglottis and the larynx are particularly endowed with inhibitory power over both the respiration and the circulation. Dragging heavily upon the tongue, swabbing out the pharynx, pressure upon the larynx, and manipulation, however gentle, of the laryngeal mucosa may cause temporary inhibition of respiration and the heart. It is true that these inhibitions usually pass off, but they affect the patient unfavorably.

When there is obstruction of respiration and the extraordinary muscles are in action, general anesthesia becomes dangerous and should never be administered. These muscles are not brought into play except when the ordinary muscles which are not paralyzed in surgical anesthesia are incompetent. Now, the extraordinary muscles are paralyzed by the anesthetic quite as readily as voluntary muscles in other parts of the body; the administration of the anesthetic, then, will paralyze muscles that are necessary for the maintenance of life; hence, general anesthesia under such a condition is absolutely contraindicated. The want of knowledge or appreciation of this small bit of surgical physiology has been responsible for many deaths. Likewise when the respiratory center is subjected to increased pressure, as in intracranial hemorrhage, abscess, tumors, etc., it is readily paralyzed. Under such circumstances anesthesia must be closely watched. In opening the skull in such cases it is sometimes necessary to do so under local anesthesia. If general anesthesia is employed, preparation should be made beforehand for artificial respiration without seriously hampering the operation, which may be proceeded with as hastily as is consistent with safety until a portion of bone is removed, relieving the pathologic tension and with it the embarrassment of the respiration. After this, anesthesia may again become safe. While the vagi play such an important rôle, it is well to remember that the division of one is followed by but little change in the general function. I have seven times in removing malignant tumors excised portions of one vagus and have not noted any alterations of consequence in the respiration. Excision of both, however, has thus far proved uniformly fatal.

The reflex phenomena in gall-stone colic from a diagnostic standpoint are most interesting. There is scarcely any subjective symptom so important as the inhibition of the diaphragm in gall-stone colic. The inhibitory path through the afferent nerves supplying the gall-bladder region, which is located in the adjoining segment in the spinal cord to that of the phrenics, to which this impulse is transferred, is the explanation of this important phenomenon. Almost every case of gall-bladder or gall-duct colic if questioned will give a history of inhibition of the diaphragm during the attack. The diagnostic importance of this symptom is increased greatly by the fact that such inhibition occurs in almost no other instance.

As long ago as 1840 Thomas Watson pointed out the cause of the increased respiratory frequency in peritonitis as being due to the inhibition of the abdominal respiratory muscles, thus diminishing the excursion of the diaphragm and lower ribs, which in turn diminishes the area of active functionating lung. The entire lung not being in use, the respirations of necessity must be increased in frequency to compensate for their shallowness. The extreme air hunger in embolism has not as yet been satisfactorily explained, but that occurring in hemorrhage and in certain degrees of shock is explained readily on the ground of diminished blood-pressure in the respiratory center. The sensitiveness of this center is strikingly illustrated in case of gunshot wounds of the head and deeper portions of the neck. Such wounds almost invariably cause temporary and sometimes permanent inhibition of respiration.

Some of the aspects of surgical physiology of the circulation and the respiration are so intimately interwoven that a brief consideration in their association will be given.

CIRCULATION AND RESPIRATION.

In certain crises, such as sudden collapse, the proper management of the circulation and the respiration presupposes a correct interpretation of their pathologic states. Impending death due to violent alterations in which nothing physically inconsistent with life exists, requires such accurate interpretation and prompt action that the selection of the wrong horn of the dilemma may mean death. It is of the utmost importance, for example, to distinguish between a sudden circulatory collapse due to paralysis of the heart from over-distention of its chambers and sudden collapse due to an acute cerebral anemia. For example, as has been shown so conclusively by Hill, when the heart-muscle has been so deeply anesthetized as to be unable to empty itself, if the patient be inverted in the head-down posture, thereby emptying by means of gravity more blood into the heart, the paralysis would be increased and the maneuver would constitute an additional exciting cause rather than a treatment. In this instance rather extensive venesection, or, better, a reversion of the patient, feet down, so that the over-distended auricles may be depleted by gravity, followed by cardiac massage, would be quite likely to enable the heart to recover its function.

If, on the other hand, acute cerebral anemia be mistaken for an acute dilatation and the patient be placed feet downward for the purpose of relieving a supposedly paralyzed heart with over-distention, the error would be equally great.

In collapse from asphyxia at its latest stages the heart is always greatly distended, partly because the state of asphyxia is attended by a marked rise in the blood-pressure due to the stimulation of the vasomotor center and partly to the loss of oxygen to the heart-muscle. In this state the supply of oxygen is the first requisite. It is well to remember that the rhythmic contractions of the heart continue for a certain length of time after the heart has become too weak to produce a pulse. The heart if examined will be found in the state of extreme over-distention. If in this condition intravenous saline infusion were given, the over-distention and paralysis would be augmented and the probability of the resumption of the heart-beat would be diminished directly in proportion to the effectiveness of the intravenous infusion. So, too, if the patient were placed in the head-down posture the over-distended heart would be filled even more, which in like manner would diminish the probability of recovery. On the other hand, rather extensive venesection, or, better still, the feet-down posture with quick massage, will relieve the heart of over-distention. The rhythmic pressure upon the thorax over the heart is alone capable of producing a moderate circulation of the blood. This, with the artificial respiration, will supply the heart some oxygenated blood. The immediate resumption of the heart-beat may follow. Following this stage of the resuscitation, if the cerebral anemia is still threatening, the patient may be gradually placed, first in the horizontal, then in the head-down posture. If, however, in any case of sudden collapse cerebral anemia is the most important consideration, the head-down posture with pressure upon the abdomen and the lower extremities should be provided.

It is well known that it is easier to reëstablish the rhythmic action of the heart than to resuscitate the vasomotor and the respiratory centers. Of these two vital centers, the respiratory is the more readily resuscitated. This center has been revived in animals even after cessation of its function for thirty minutes. There is thus far no record in experimental research of the resuscitation of the vasomotor center after the lapse of more than fifteen minutes. The heart has been resuscitated at various periods after it has ceased beating. Kuliabio was able to produce rhythmic contractions of the heart forty-four hours after death. This is accomplished by circulating through the coronary vessels warm oxygenated blood-serum at a pressure above 30 mm. of mercury. The heart resumes rhythmic beating, as a rule, when oxygenated blood under a pressure of 30 mm. or more circulates through the coronary vessels. The first problem, then, that confronts us is the establishment of such a circulation through the coronary vessels. This cannot be done by intravenous infusion alone, because the vascular tone being entirely lost it is quite impossible to cause the circulation by this method through the coronary vessels at such a pressure. Massage of the heart is effective, but here too, the periphery being entirely relaxed, it is extremely difficult to establish a blood-pressure of more than 15 or 20 mm. In many instances the mean blood-pressure cannot be raised more than 10 mm. The obvious lack, then, is the peripheral resistance. This may in many instances be amply supplied by the intravenous administration of adrenalin or other blood-pressure raising principles of the suprarenal glands.

The adrenalin may be injected directly into a vein; it may be given by inserting the needle of the hypodermic syringe into the rubber tubing of the intravenous infusion apparatus while the stream of saline fluid is flowing, or it may be mixed with the saline solution. This mode of introduction assures the flow of adrenalin toward or to the auricles. Now, adrenalin applied to blood-vessels after death still causes their contraction. This is easily demonstrated even an hour after death. By maintaining cardiac massage, which in itself may produce a very considerable circulation, the adrenalin is distributed over a certain vascular area. Its constricting action upon the vessels to which it is thus distributed causes a certain peripheral resistance, giving the first real basis for the establishment of an increased blood-pressure. By proper massage, the circulation, and hence the distribution of adrenalin, is increased. There is then an increase in the area of vascular contraction, therefore an increase in the peripheral resistance, producing an increase in the blood-pressure in the various arteries, and in none more so than in the coronary. After the blood-pressure in the coronary artery has reached 30 mm. or more the heart will most likely resume its rhythmic contractions. As soon as the rhythmic contractions are well established further massage would better be withheld and the circulation favored by gravity, the patient being placed in the head-down posture. In addition, the lower extremities and the abdomen should be rapidly bandaged or the rubber pneumatic suit should be applied and inflated so that the peripheral resistance may be artificially increased until the vasomotor center has received a sufficient amount of circulation under a given pressure to cause the resumption of its normal physiologic action. About this time the first signs of respiratory recovery will be noted, usually by a very faint inspiratory action in which the diaphragm alone will act. The first contraction of the diaphragm is so slight as scarcely to be noted. The pause will be quite long, then comes the second contraction of the diaphragm, slightly stronger, and so on. Each succeeding contraction becomes more effective. Then the intercostal and the accessory muscles come into play soon after a normal respiratory rhythm appears. In the process of resuscitation one must always note carefully the cardiac action, as the weakened heart muscle may be unable to cope with the suddenly increased blood-pressure. This inability may result in a sudden paralysis from over-distention. In this event it is necessary promptly to inaugurate the treatment heretofore described.

Since the widespread introduction of electricity for power and illuminating purposes, many instances of sudden suspension of animation from powerful electric currents have occurred.

In a recent research by Dr. Macleod and myself we have been able to show that there is a marked and most important distinction between the cases in which the collapse is due to the passing of the current through the heart-muscle, and those in which the current passed through the inhibitory mechanism. A study of the physiologic effects of high-tension currents upon the various tissues and organs has shown that, aside from the burning at the point of contact, no chemical changes of importance occur. That is to say, in an animal permitted to recover, through whose head 2300 volts of an alternating current had been passed there was no discoverable loss of function during an observation of more than a month after the experiment. The blood is unaltered by such high-tension currents. In the cases in which the current was passed through the head and neck and not the thorax, or in which it was passed from the head to the fore-limb, the heart was suddenly stopped. In the experiments in which the animals were given a physiologic dose of atropin prior to the experiment, causing a paralysis of the terminals of the vagi in the heart, the inhibitory effect of the strongest current was almost wholly obviated. Then, too, the animals in which there was a sudden cessation of cardiac action through inhibition were readily resuscitated. When, however, the current passed directly through the heart-muscle itself, fibrillary contractions of the heart were produced, causing in every instance death, and in no instance was resuscitation possible.

It would follow, then, that in the sudden collapse from inhibition resuscitation may readily be accomplished by immediate rhythmic pressure upon the thorax over the heart. This pressure produces not only an artificial circulation but artificial respiration as well; the latter, however, only provided that the tongue be drawn well forward, giving free space for the exchange of air. It would be quite rare that a physician could reach the scene of such an accident in time to be of assistance, but this information in the hands of fellow-workmen may be easily turned into life-saving practice.

MUSCULAR SYSTEM.

Muscle fibers are at all times, in the normal state, under a certain though light degree of tension. This tension is known as muscular tone. Muscular tone continues in the sleeping as well as in the waking hours. Muscular tone is very frequently increased or diminished either from general or local causes. A decrease in the general muscular tone is due to the usual causes of general depression, such as old age, wasting disease, fatigue, anemia, hemorrhage, shock, certain drugs, anesthetics, etc. A local decrease in muscular tone may be due to loss of nerve- or blood-supply, by warmth, and very markedly in antagonistic muscles during the contraction of their opponents. For example, during the contraction of an extensor muscle the corresponding flexor loses its muscular tone, so as to allow free extension and vice versa. This quality may frequently be made use of in surgical procedures. The local effect of heat in causing a diminished muscular tone is an operation as old as surgery itself. The most perfect examples of the loss of muscular tone occur in fracture dislocations involving the severing of the spinal cord. The flabby muscles of the paralyzed part are so characteristic as to be almost diagnostic of the lesion.

In deep alcoholism muscular tone is greatly reduced, and in this state the viscera are sometimes subjected to serious trauma. The muscular tone of the abdomen and lower thorax is such as to protect the heart fairly well against mechanical violence. In deep alcoholic intoxication there have been many instances of marked collapse and occasional death from blows or from encountering corners of tables, etc. In this state the loss of muscular tone permits the ready depression of the lower ribs, exposing the heart to direct trauma. The loss of the tone of the muscles of the pharynx and tongue is noisily indicated in the loud snoring sleep of the drunkard.

After certain operations requiring wide incision, such as nephrectomies and operations for certain tumors or abscesses, nerve-trunks may be divided, causing loss of muscular tone over the area they normally supply. This is easily observed in the quiescent state in the upright posture as a diffused bulging. It is markedly accentuated in coughing or in any form of increased intra-abdominal pressure. In some instances it might almost be designated as a diffused hernia of the abdominal wall. Increased general muscular tone usually coincides with a state of exalted vitality, such as is produced by the action of certain drugs; for instance, strychnin. Local increased muscular tone is of great importance from the surgical standpoint.

In all injuries such as fractures, dislocations, contusions, the muscular tone of the area involved is usually markedly increased. Often this becomes a most important surgical factor. This is most difficult to cope with in the treatment of certain fractures, and in the reduction of dislocations. Among the brilliant contributions of Percival Pott few were more important than his work on the surgical physiology of muscles in fractures and dislocations. In the treatment of dislocations I have been able to make most effective use of our knowledge of this subject. It is easily shown that in what is known as surgical anesthesia under chloroform and ether muscular tone is impaired but not lost. Now, in dislocations the entire group of muscles involved is usually markedly increased in tension. With each effort at reduction the goading of the injured part causes an increase in this tension, so that the surgeon is constantly exciting a resistance proportionate to his efforts at reduction at least up to the functional capacity of the muscles. It was on this ground that the heavy traction and great mechanical methods were introduced in the reduction of dislocations. Such a dislocation involves often very extensive additional injury to the surrounding parts. So long as muscular tone remains even under anesthesia, the manipulation of the injured parts causes an increase in the muscular tension. Therefore anesthesia, that is, ordinary surgical anesthesia, is only partially effective in overcoming the obstacles for the reduction of dislocations. If the anesthetic, however, is pushed beyond the depth suitable for surgical operations, that is, if it is pushed until muscular tone is lost, the reduction of recent dislocations in which there is no mechanical difficulty involved becomes the simplest possible matter, producing almost no additional trauma.

With ether anesthesia it is necessary to continue its administration until sharp tapping of the abdominal muscles elicits no reflex, that is to say, until the abdominal muscles are precisely similar in their relaxation to their state when the spinal cord has been severed. In anesthetizing to this depth one must reckon at the start with the relaxation of the pharyngeal muscles, requiring the tongue to be drawn out and the most advantageous position of the head and jaw maintained. I have never been able to abolish the muscular tone without causing deep snoring. It is obvious that the muscular tone of all the muscles must be overcome, hence the pharyngeal, as a matter of course, must become so relaxed as to cause some obstruction to respiration. It usually requires about ten minutes of anesthesia before this state of complete abolition of muscular tone is reached. It is quite important not to make any attempt at reduction before complete loss of tone is established. If this is done, the local tone is so markedly heightened that an increased amount of anesthetic is required. The abdominal reflex is a uniform guide. By this method dislocations in which attempts at reduction by main force under ordinary anesthesia had been made without result, for an hour or more, have been reduced by the simplest manipulation without the use of much more force than is necessary to lift the limb. The simplicity and the effectiveness of the method when first used are most striking.

Increased muscular tension to secure physiologic rest in the region of inflammations is a conservative process. This phenomenon is in many instances a diagnostic sign of great importance. The fixation by muscular tension of the neck, the spine, the hip-joint, the knee-joint, in acute and tuberculous infections is a common example. The same is true of the intercostal muscles in pleurisy and of the abdominal muscles in peritonitis. In the latter case the diagnostic value is of even greater importance, because the lesion is so frequently deep-seated as to be difficult of recognition. That this increased muscular tension is not due to voluntary action is proved by its presence, though modified, in complete surgical anesthesia. If closely observed, almost every grade of peritonitis is attended by a corresponding degree of increased muscular tension. Indeed, the gradation from the normal muscular tone up to the diffuse board-like rigidity is so gradual that one would be quite unable to state where normal muscular tone left off and pathologic tension began, the whole seeming to be an exaggeration of the normal physiologic state of muscular tone. At the very beginning of increased muscular tension the alterations may be so slight that only by the most careful observations, especially by making comparisons with neighboring normal regions, can the pathologic increase be definitely determined. This increase constitutes a definite sign.

It is interesting to note that whereas the normal recti, so far as we know, act as a whole, these muscles may present a state of segmental rigidity. In peritonitis, distinctly localized, a single zone of the rectus may present pathologic tension while the remainder of the muscle may be quite normal.

Under the surgical physiology of the respiration it was pointed out how the increased tension and fixation of the muscles of the abdomen modified the various functions, such as breathing, coughing, sighing, speaking, urination, defecation, and, in short, all the physiologic acts involving an increased intra-abdominal tension. The description of this state by Thomas Watson as long ago as 1840 remains a classic.

PHYSIOLOGIC COMPENSATIONS.

That wonderful attribute of vital force whereby one organ may compensate for another is one of the most reliable foundation-stones upon which surgical practice rests. One muscle may compensate for another or a group, and a part of a muscle for the whole; the loss of bones and joints may be compensated for by minimizing some function here and exalting others there; a portion of one lung may compensate for both; one kidney, for the other. In laryngectomy the mouth finds new vocal cords;

in gastrectomy the function of the stomach is assumed by the intestines, and for the loss of the greater part of the latter, compensations have been provided. The rectum may act for the bladder; the abdominal muscles, for a sphincter ani. Ductless glands and bone-marrow reciprocate in times of physiologic distress. The range of compensation in injury and disease of the heart by virtue of the compensatory assistance of the great thoracic pump,—the respiratory system,—which alone is capable of producing a moderate circulation, is most important in operations in this region. In acute hemorrhage the quickened circulation and increased respiration, together with reabsorption of fluids from the tissues, compensate for the loss of blood. The effect of occlusion of the largest arteries and veins may be counteracted by the combined compensatory effort of innumerable smaller vessels. The range of compensation is so large that it is truly difficult to handicap an organ or physiologically to incapacitate a vitally strong man.

BLOOD-PRESSURE.

The determination of the blood-pressure in the human being for the purpose of clinical study has been variously contemplated by a number of different observers. All these methods have for their basic principle the force that is required for the obliteration of the pulse, this being directly derived from the common usage of measuring the arterial tension by means of digital compression. Vierordt, in 1885, is stated to have measured more accurately the force required for the obliteration of the pulse, by means of a sphygmograph, of which he stated that absolute values, as to the tension of the arteries, could not be obtained.

Kries, in 1875, determined the capillary tension in the human being by causing a pallor of the integument, by means of the pressure of known weights. Marey, in 1876, applied the same principle, by enclosing the entire arm in a glass cylinder, then compressing the contained air to a point sufficient to produce pallor. The blood-pressure, as determined by this method, corresponded to a point midway between the pressure of pallor and of flushing. In later investigations hydrostatic pressure was employed instead of air-pressure, as well as a mercury manometer for the registration of the oscillation of the pulse. The maximum pressure was then determined by increasing the pressure till all oscillations of the pulse ceased. According to later investigators, this method is stated to be quite faulty (Breuer, Basch, Recklinghausen).

In still later attempts Marey inserted only a finger in a cylinder; this seemingly did not insure greater efficiency.

Ray and Brown, in 1878, then measured the blood-pressure by placing a membrane, stretched over a capsule, upon the skin and applying air-pressure or water-pressure. The capsule was connected with a water manometer. A distinct advantage is stated to be possessed by this method, as the obliteration of the vessels could be accurately determined macroscopically. Waldenburg, in 1880, again employed the method of Vierordt, rendering it somewhat more serviceable.

Among the methods which have since appeared, all of which have been variously employed by the different investigators, there are: The method of v. Basch, 1881; of Mosso, 1895; of Hurthle, 1896; of Riva-Rocci, 1896; of Hoepfle, 1896; of Hill and Bernard, 1898; of Oliver, 1899; of Gaertner, 1899; of Stanton, 1903; and of Janeway.

Only a few of the more commonly used instruments will be described.

The Riva-Rocci sphygmomanometer (Fig. 15), as described by Stanton, consists essentially of three parts: "A flat rubber bag or tube, about 40 cm. in length and 4 cm. in width, covered on the outer surface with canvas, to prevent expansion outward. One end of this tube is kept permanently closed by the special clamp, while the other end is pressed by a lever, worked with a screw adjustment, after the tube has been properly fitted to the upper arm of the patient. A metal tube passing through the clamp serves to connect the interior of the tube to the remainder of the apparatus. The second part is a mercury manometer, the scale of which will register at least 300 mm. The third part is the air-pipe, which in this case is a rubber syringe of the type furnished with the thermocautery (Cushing's modification). These three parts are connected to three limbs of a four-way glass connection. To the fourth limb is attached a short rubber tube closed with a spring clip, by means of which the air can be allowed to escape after the pressure has been determined." In the application of this instrument the rubber armlet is fitted around the arm above the elbow, the muscles being in a state of relaxation and the constriction occurring at about a level with the heart. As the air enters the armlet, it compresses the arm with a force that is measured by the height of the mercury column, and this compression is transmitted through the soft tissues to the artery. As

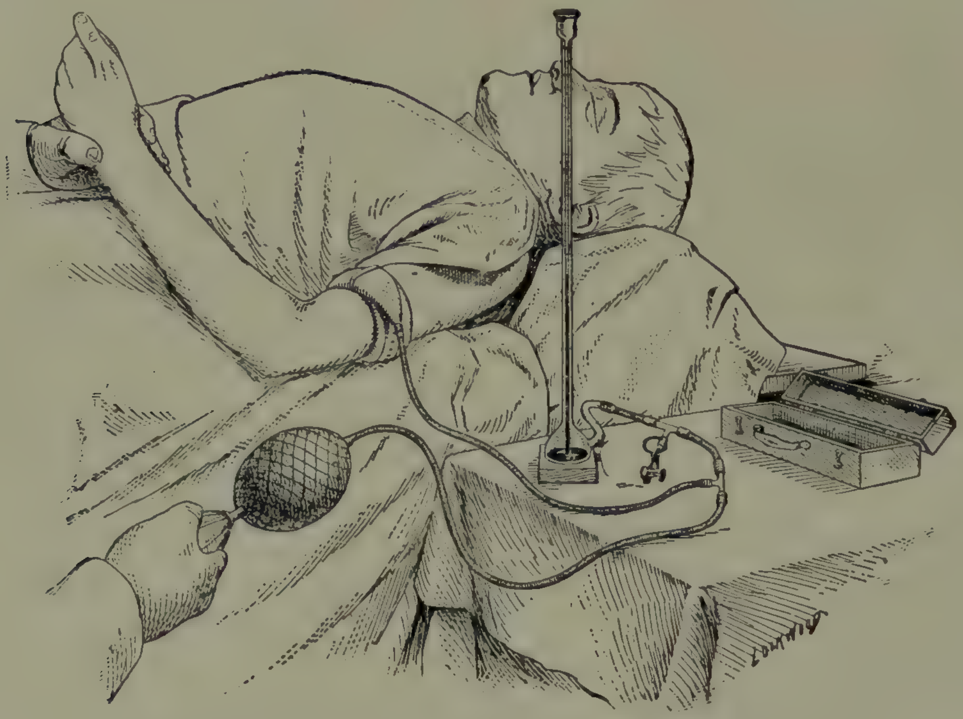

FIG. 15.—RIVA-ROCCI SPHYGMOMANOMETER AS MODIFIED BY COOK.

the pressure increases, the pulse disappears. Either this point of disappearance of the pulse, or the point at which the pulse reappears after compression, is read off the manometer scale as the pressure. Cushing's modification of the Riva-Rocci instrument, whereby a thermocautery bulb for rapid inflation and a special clip for releasing the pressure are added, renders more frequent observations possible and greatly increases its usefulness.

Stanton's method (Fig. 16) consists of a rubber arm in which the width of the compressing surface is more than twice as large as that of the Riva-Rocci or the Hill-Barnard methods (3¼ inches wide and 16 inches long). This rubber cuff is prevented from expanding outward by a cuff of leather or of double thick canvas reinforced by tin strips. "To the center of the rubber cuff is cemented a rubber valve-stem of the kind used on the inner tube of a bicycle tire, through which passes a glass connecting tube, its extremity being flush with the inner surface of the armlet. A piece of stiff-walled rubber tubing, about one-fourth inch in caliber, connects the glass tube in the valve-stem with one end of the horizontal limb of a glass 'T', while a similar piece of tubing joins the other extremity of the horizontal limb to a mercury manometer. The vertical limb of the 'T' is connected by a softer tubing of the small pump." To determine the blood-pressure by this method, the rubber armlet is fitted to the arm above the elbow and air is forced through the apparatus until the pulse is no longer palpable. The air is then permitted to escape through the soft tube, which is held by the fingers until the pulse reappears, and this

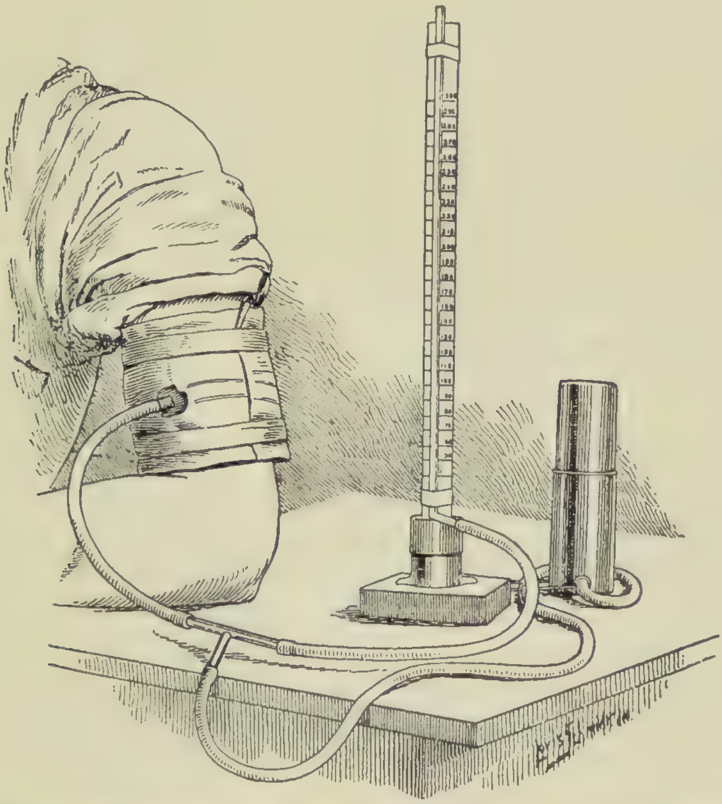

FIG. 16.—STANTON'S METHOD FOR THE DETERMINATION OF BLOOD-PRESSURE.

point is mentally noted as the systolic pressure. The pressure is now reduced a few millimeters at a time, and the pulsation in the mercury column will increase in size until a maximum is obtained, then diminish. The base-line of these maximum pulsations is noted as diastolic pressure. The mean pressure is the mathematical mean of the two pressures obtained.

Janeway's modification is shown in the accompanying figure (Fig. 17).

It will be seen from the description of the various instruments that the general construction and method of all are similar, the essential parts being a manometer, a compressing armlet, and an inflating apparatus. The general method of use, according to Janeway, may be described as follows: "The armlet is fastened snugly about the arm or thigh at the level of the heart. On the thigh this necessitates the recumbent posture. The finger ordinarily used for palpating the pulse is then placed on the radial, or the dorsalis pedis, and the patient instructed to relax the limb completely. With the other hand the pressure is then raised steadily by means of the inflating apparatus. When the volume of the pulse begins to diminish, the pressure is increased very slowly until the pulse disappears, then released as gradually as possible until its return is detected. The height of the manometer column at which this occurs is noted, and the pressure raised just enough to again obliterate the pulse. It is allowed to fall a second time and another reading made. If the two points correspond within 5 mm. of one another, the average may be taken

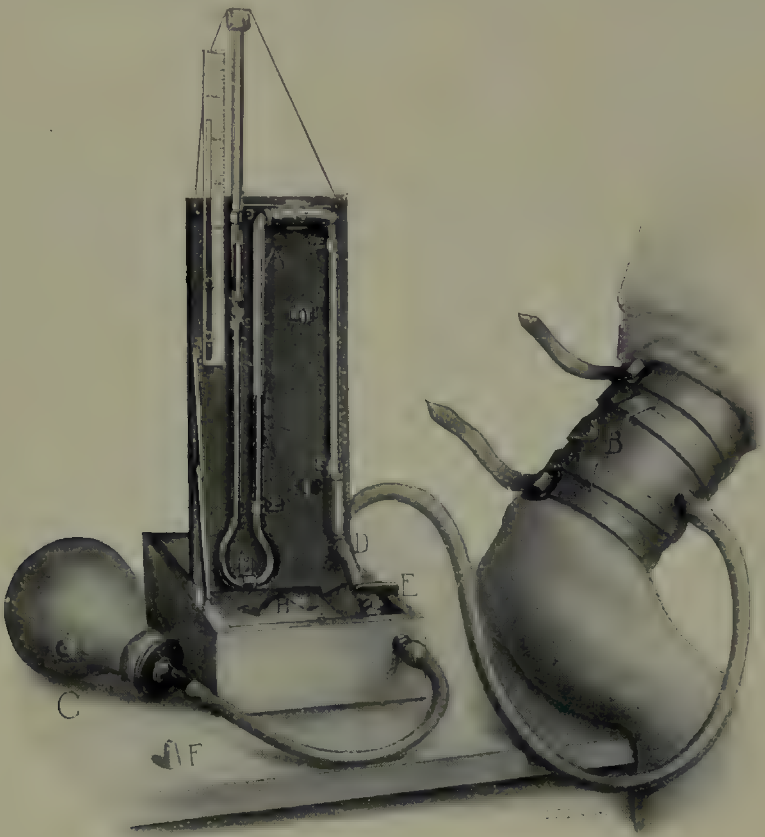

FIG. 17.—JANEWAY'S SPHYGMOMANOMETER.

as the systolic blood-pressure at the time of observation. If the readings fail to approximate so nearly, one must wait a couple of minutes and determine anew."

In estimating the clinical value of blood-pressure determinations, consideration must be given to the following questions: Is there a normal standard of blood-pressure in the same species? How great are the individual variations? Are there variations of consequence in the same individual? Are the causes of the individual variations such as will likely interfere with correct determinations? Have we the means of making accurate determinations of the human blood-pressure? Are the variations in clinical cases of importance?

In my surgical laboratory accurate arterial pressure under full anesthesia was recorded on one hundred normal dogs. The minimum pressure was 80; the maximum pressure, 170; the medium pressure, 125. The weight of the animals and their blood-pressure bore no relation to each other. It was impossible to estimate the blood-pressure of a given animal. Often a small cur showed a higher pressure than a Newfoundland, or a fox-terrier higher than a bull-dog. In continuous observations upon the blood-pressure of the same animal marked variations were noted. This was true in the animals in which ether anesthesia, morphin anesthesia, or curare was administered. It was not possible by the closest observation to predict the changes at any moment. These normal changes in pressure varied from a few to 20 mm. Hg. In some instances the changes were abrupt; in others they were gradual.

The duration of the changes varied. These variations, which have been proved to be mainly vasomotor, were prominent in the normal animal. After the blood-pressure had been reduced very considerably, the changes were less marked. The nearer the fatal point was reached in the fall of the blood-pressure, the less marked were the changes; but when the blood-pressure had fallen to such a degree that the vasomotor changes were not so marked, the effect of respiratory action upon the blood-pressure curve was increased. In some extreme instances in these low blood-pressures the variation during each respiratory action was more than half that of the entire blood-pressure.

The difference between the systolic and the diastolic pressure in normal animals varied greatly. In the development of shock the difference between the systolic and the diastolic pressure was diminished; that is to say, there was a decrease in the height of the pulse-wave. In asphyxia in reflex inhibition, in the administration of saline infusion, in cerebral compression, the pulse-wave was increased in length. The most marked difference between the systolic and the diastolic pressure occurred in the experiments in which saline infusion was rapidly administered after the animals had been reduced to a profound degree of shock or collapse. In making human blood-pressure determinations on normal individuals marked individual differences were noted. These differences not only appeared in different ages and psychic states, but also in subjects of the same age and virtually under the same conditions. To determine more accurately these conditions, observations were made on the inmates of the Protestant Orphan Asylum, in which the conditions were as nearly equal as could be obtained. Here individual variations were still marked. Similar results were obtained in blood-pressure determinations upon the aged. In making repeated determinations in the same individual, it was found that the physical state, such as exercise, the ingestion of food, sleep, fatigue, etc., all caused variations. The psychic state caused in some instances a variation of 40 or more mm. Hg. Fear, anxiety, self-consciousness, all caused a rise in the blood-pressure. While experimenting upon the pneumatic rubber suit it was very difficult to find any one not under an anesthetic who did not exhibit a marked rise in the blood-pressure while the suit was being applied, and before any pneumatic pressure had been exerted. These psychic changes were so marked that our observations on any except the anesthetized were not regarded as accurate. In following the blood-pressure under full anesthesia, when non-operative procedures were in progress, considerable change was noted. Normal subjects, even in a quiet horizontal posture, without apparent cause showed variations, although usually slight. By giving close attention, the variation in pressure occurring with each respiratory excursion could be occasionally noted.

The accuracy of the various instruments thus far devised is only relative. This is particularly true in the determination of the diastolic pressure. The coefficient of error is diminished with the increase in skill and experience in the use of the instrument.

CLINICAL REMARKS ON BLOOD-PRESSURE.

Blood-pressure determinations by the instruments and the methods now in vogue are only relatively accurate. Among the sources of error are:

(*a*) *Individual Factor.*—The difference in the keenness of the tactile sense in various observers, frequently amounting to several millimeters in equally experienced observers, must be taken into account; even the same observer may record slight variations in separate observations.

(*b*) *Mechanical.*—The size of the limb on which the observation is made is a source of slight error. In a large limb the observation is slightly less accurate than in a smaller. The width of the encircling band should vary with the size of the limb. The slight resistance of atheromatous vessels should not be neglected.

(*c*) *Physiologic.*—The normal blood-pressure is ever fluctuating. With each respiratory excursion the blood-pressure varies. Should the disappearance of the pulse be noted at the end of the inspiratory or at the beginning of the expiratory phase, the pressure would be recorded higher than if observed at the end of the expiratory, or the beginning of the inspiratory. It is well, therefore, to note the respiratory factor. The lower the blood-pressure, the more marked is the fluctuation during the respiratory phases. If, in addition, there is labored respiration, the source of the error is correspondingly increased.

The psychic factor is always to be considered. I have repeatedly observed wide alterations due to the interest and mild excitement incident to the mere taking of a blood-pressure observation—purely a psychic factor. A recent meal, exercise, smoking, drinking, etc., may produce temporary changes in the blood-pressure.

Despite these various sources of error, the method is incontestably more accurate than a pulse observation as ordinarily taken. Then, too, as a means of recording the blood-pressure it is more accurate than any possible description of the pulse by such relative terms as "soft," "hard," "full," "high tension," "easily compressible," etc. By charting the blood-pressure, determinations approach an exact method in record keeping.

From a practical standpoint it is not necessary to use it as a routine except as a training for students, internes, etc.

Clinically, blood-pressure observations are of importance in rather specialized instances.

CLINICAL APPLICATION IN OPERATIVE SURGERY.

To accumulate physiologic data and to determine the value of blood-pressure observations during operations in my service, Dr. C. E. Ford and others made observations for me during 1000 surgical operations. After an extended experience Dr. Ford was able to estimate offhand with remarkable accuracy the pulse tension. The constant checking of the conventional pulse observation by a manometer soon corrects the common errors and, in a measure, standardizes pulse observation.

Head. — *Trephining.* — Incising the scalp caused no notable change in the blood-pressure. Separating the periosteum over a considerable area of bone by means of a periosteotome caused a slight irregularity. Cutting through the bone by means of a mallet and a chisel caused some irregularity, although no marked net change was noted. Irritation of the dura caused a fall with considerable irregularity. In an operation for securing hemorrhage from a branch of the meningeal considerable manipulation was necessary. In order to control the hemorrhage during the removal of more skull, gauze was packed between the skull and dura some distance beyond the margin of the bone; this caused a very considerable fall in the blood-pressure. Exploring the brain for a tumor by means of a slender probe caused an appreciable change. A similar observation was made in exploring both lobes of the cerebellum in like manner for a tumor. The incision of the dura with a sharp knife caused no appreciable change. Sponging with pressure caused the most marked fall.

In operations for the removal of the Gasserian ganglion, the blood-pressure and the pulse showed marked variations without any considerable net change until the skull was opened.

In the cases in which these observations were made the common carotid artery was closed and the hemorrhage up to the point of making the intracranial dissection was practically nil. Elevating the dura caused an irregular fall in the pressure and an increase in the pulse-rate. Separating with considerable gentleness the branches and the body of the ganglion caused no marked change. Elevating the temporo-sphenoidal lobe in order to give room for the exposure and removal of the ganglion caused a marked rise in the blood-pressure and an almost corresponding fall in the pulse-rate (Fig. 18). These phenomena were strikingly shown in several of Cushing's cases. During this part of the operation there was some oozing; against this adrenalin tampons were used. A considerable rise in blood-pressure in one case followed, due probably to absorption of adrenalin. The most rapid fall in the blood-pressure in the cerebral group occurred in a case in which there was a rapid hemorrhage from the meningeal artery, which was controlled by gauze packing. The combined effect of the hemorrhage, the irritation of the dura mater, and the pressure on the brain caused a rapid fall. The blood-pressure changes in operations upon the head are proportionate to the manipulation, the pressure upon the brain, the hemorrhage, and the duration of the operation.

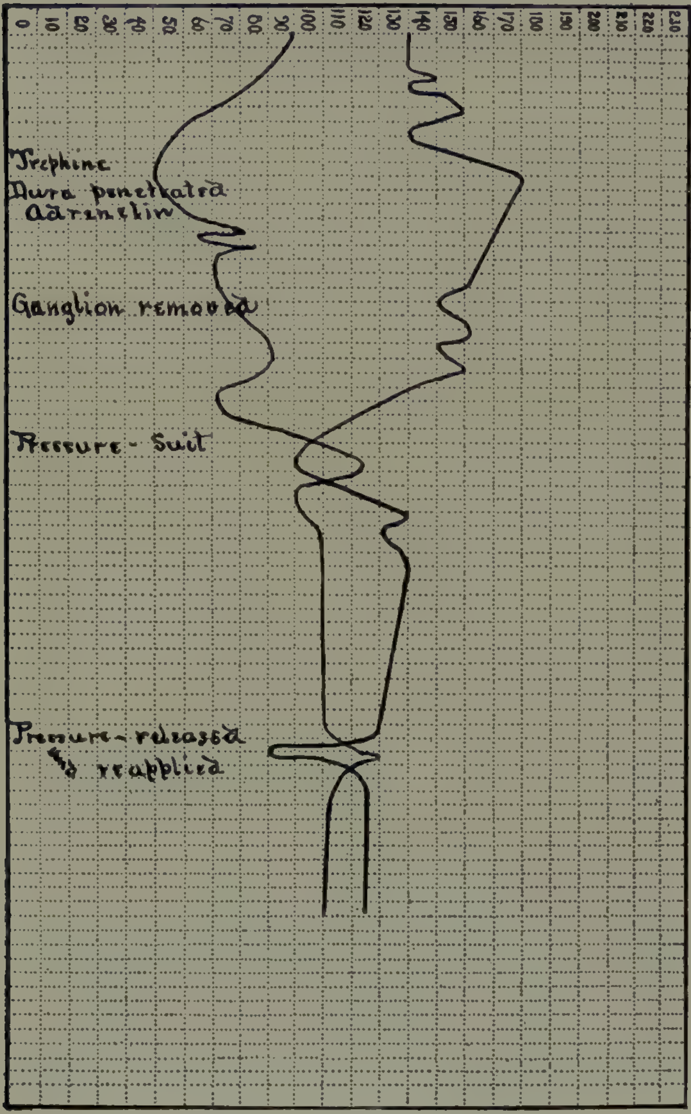

FIG. 18.—EXCISION OF THE GASSERIAN GANGLION.

Note the rise in the blood-pressure and the fall in the pulse-rate while the ganglion was being extracted. On the completion of the operation the blood-pressure fell to 100 mm. The patient during the operation was in a semi-sitting posture to minimize the venous hemorrhage. The rubber suit was then inflated until the blood-pressure again reached 140 mm., the level before the operation. After two hours the pressure in the pneumatic suit was released. The blood-pressure immediately fell 40 mm. The pneumatic suit was then inflated until the blood-pressure rose to 124 mm. and there maintained until the shock disappeared.

Mouth.—In bloodless excision of the tongue and in operations on the floor of the mouth there was but little change in the blood-pressure or the pulse.

Neck.—*Tracheotomy.*—Asphyxia caused a very marked rise in the blood-pressure, and slowing of the pulse-rate. In one case the unusual opportunity presented itself of making observations upon the blood-pressure just before and during the development of asphyxia. The blood-pressure rose abruptly from 150 mm. to 220 mm. Hg. Immediately upon opening the trachea and producing artificial respiration, the blood-pressure fell to 140 mm. and the pulse became more rapid than normal (Fig. 19). The character of the pulse, both as to quality and rate, underwent as rapid changes as the blood-pressure.

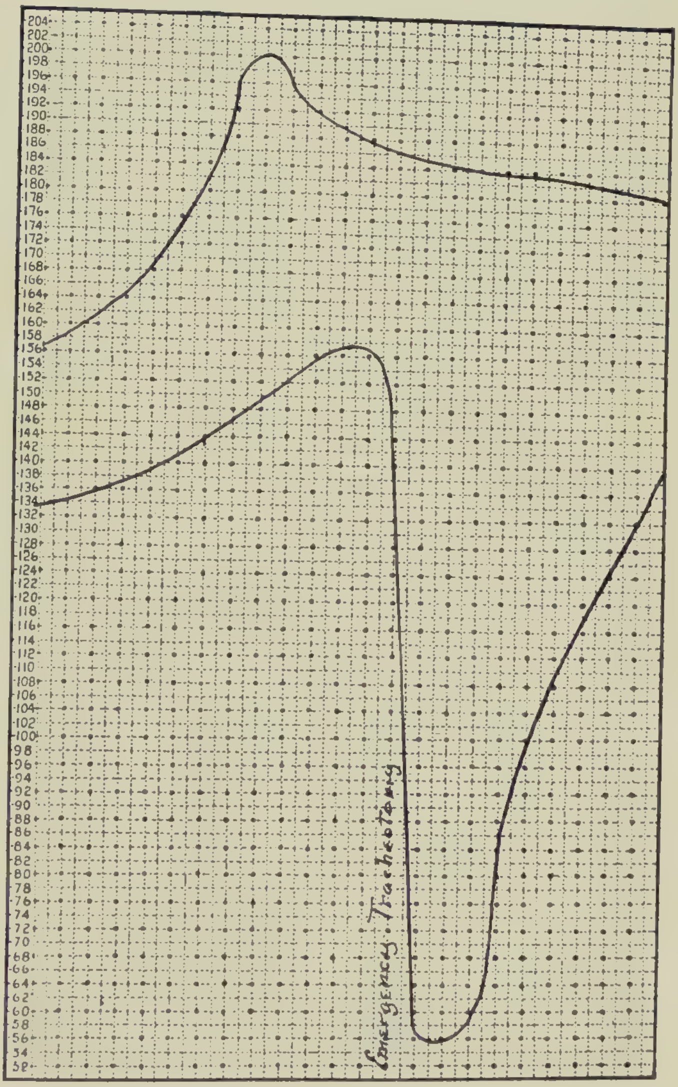

FIG. 19.—CASE OF EXTREME ASPHYXIA.

Note the fall in the pulse-rate and the rise in the blood-pressure. Note the rapid recovery after tracheotomy.

Tracheotomy under cocain in the absence of asphyxia is attended by no special changes in the blood-pressure.

In laryngeal operations the mucosa and the superior laryngeal nerves were cocainized; under these conditions, opening the box of the larynx, explorations of the interior of the larynx, and even laryngectomy caused no marked rise in the blood-pressure. In one instance, while dissecting out glands lying close to it, the superior laryngeal nerve was subjected to traction. This was attended by an immediate fall in blood-pressure and a marked slowing of the heart (Fig. 20). Both were due to reflex inhibition from mechanical stimulation. In one instance a papilloma which filled the entire box of the larynx and extended up to and over the entire under surface of the epiglottis was removed without any marked change in the blood-pressure.

In operations for removal of tumors of the neck, blood-pressure changes were proportional to the loss of blood, to the mechanical insult to the tissues, to the manipulation of certain nerve-trunks, and to the duration of the operation. In removing tumors of the parotid it was found in two instances that while dissecting them out of their bed, in the deep angle behind the jaw, a marked rise and sudden fall in the blood-pressure and in the pulse-rate occurred. As soon as the change was noted the area was packed with cocain. After this, by more careful manipulation, and from the effects of the cocain, the tumors were removed without producing further alteration. Excision of such muscles as the sternomastoid caused no marked change. Quick division of the vagus caused no effect upon the blood-pressure or pulse, but rough manipulation and traction caused a considerable fall. Observations were made upon eleven sections of the vagus. Dissections involving the exposure and manipulation of the sympathetic nerve-trunks caused an increase in pulse-rate. Resection of the trachea and of the esophagus caused no marked change. There were no immediate effects following temporary or permanent closure of the carotid artery.

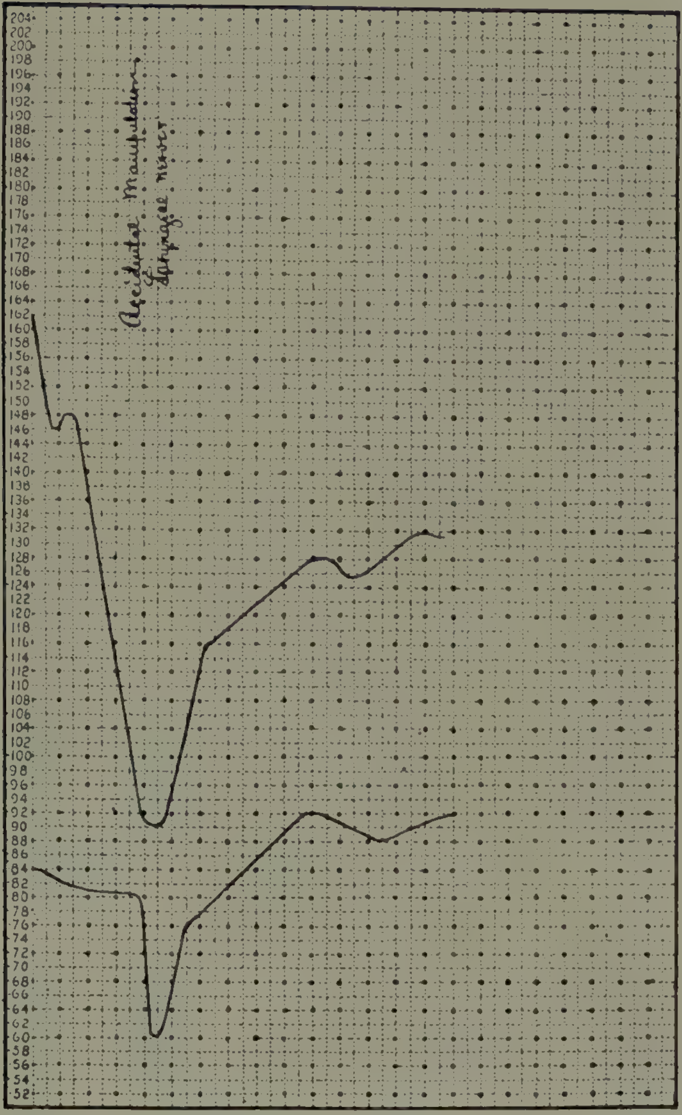

FIG. 20.—PHASE SHOWING THE EFFECT OF AN ACCIDENTAL SEVERE MANIPULATION OF THE SUPERIOR LARYNGEAL NERVE IN A LARYNGECTOMY.

Note the marked fall in the pulse-rate and in the blood-pressure. The nerve was then identified, cocainized, and severed, after which the pulse and pressure ran an even course, the pneumatic suit supporting the circulation.

Observations upon the blood-pressure during the removal of five branchiogenic carcinomata, in which all the structures above mentioned were removed *en bloc*, gave the opportunity for making the observations. In removal of branchial cysts but little change in the blood-pressure was noted. In operations for the removal of tuberculous glands the amount of shock was proportional to the vitality of the patient, the duration of the operation, the amount of loss of blood, and the amount of mechanical irritation.

In a case of sarcoma projecting from the thorax into the lower portion of the neck, exhibiting a misleading amount of mobility, removal was attempted. It was not discovered, until the dissection had proceeded so far that hemorrhage underneath and behind the tumor could not be controlled, that it should have been regarded as an inoperable case. In pushing this dissection to its conclusion the clavicle was resected, the pleural cavity opened, and the brachial plexus partially removed. In this operation a rapid decline in the blood-pressure was noted. In the manipulation for dislodging the tumor from its deep bed the brachial plexus was roughly manipulated, several trunks severed, and great hemorrhage incurred. During this time the blood-pressure fell rapidly to 68 mm. The pneumatic rubber suit was then inflated, bringing the pressure to 110 mm., at which point it was maintained during the remainder of the operation (Fig. 21). In the removal of large tumors, in which hemorrhage was controlled by closing the carotid artery with a special clamp, in which a preliminary injection of atropin to protect against reflex inhibition of the heart was given, in which sharp dissection and gentle retraction instead of blunt dissection was largely made, and in which when branches of the vagus were involved inhibitory impulses were prevented by the use of cocain, only slight changes in the blood-pressure were noted. In all these serious operations the rubber suit was put on before beginning, and, as occasion demanded, the blood-pressure was supported so as to maintain a certain level.

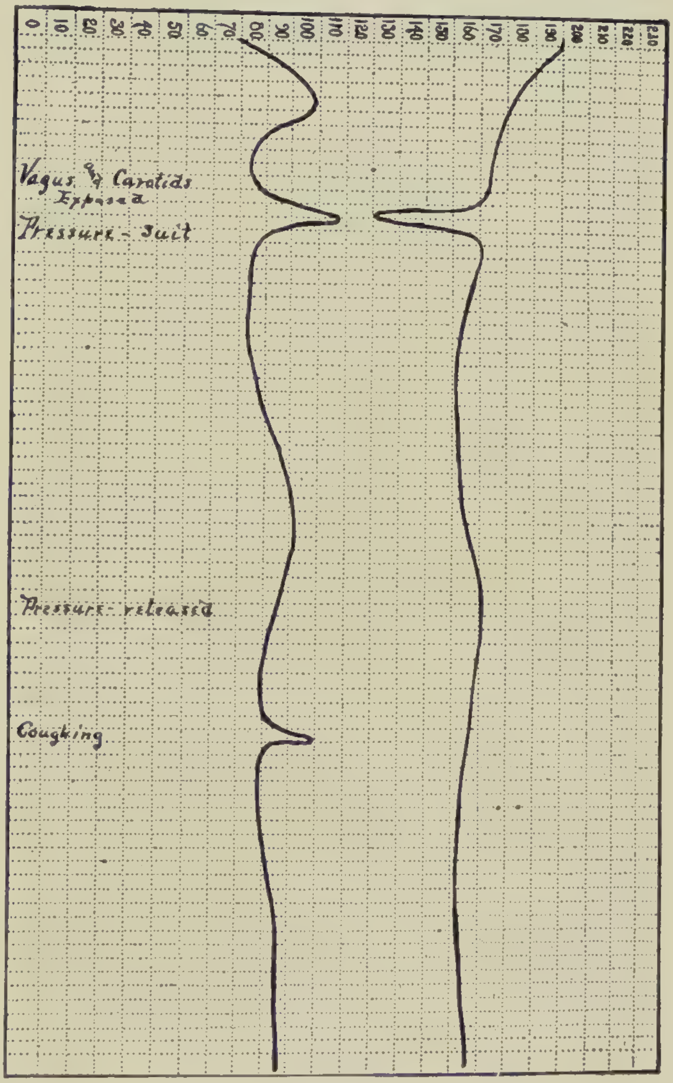

FIG. 21.—NOTE THE RAPID RISE AND EVEN MAINTENANCE OF THE BLOOD-PRESSURE ON INFLATING THE RUBBER SUIT AFTER THE MARKED FALL IN THE PRESSURE DURING DEEP DISSECTION OF THE NECK.

Thorax.—Excision of the breast for carcinoma in middle-aged subjects was attended by only moderate changes. The blood-pressure sometimes showed a decline toward the close of the operation and the pulse became proportionately accelerated. In an elderly patient a marked fall was noted. In the complete dissection of the axilla, particularly when the large blood-vessels and the nerve-trunks are involved in the dissection, the principal change in the blood-pressure was noted, the net result of which was an irregular decline.

Dissection with a sharp knife, with minimum traction, caused the least change. Rough sponging, blunt dissection, and strong retraction caused the most marked change. Resection of ribs caused but slight change, though opening the pleural cavity caused a marked change. In operation for empyema the opening of the cavity and the discharge of the pus were attended by a rapid fall in the blood-pressure and an increase in the pulse-rate.

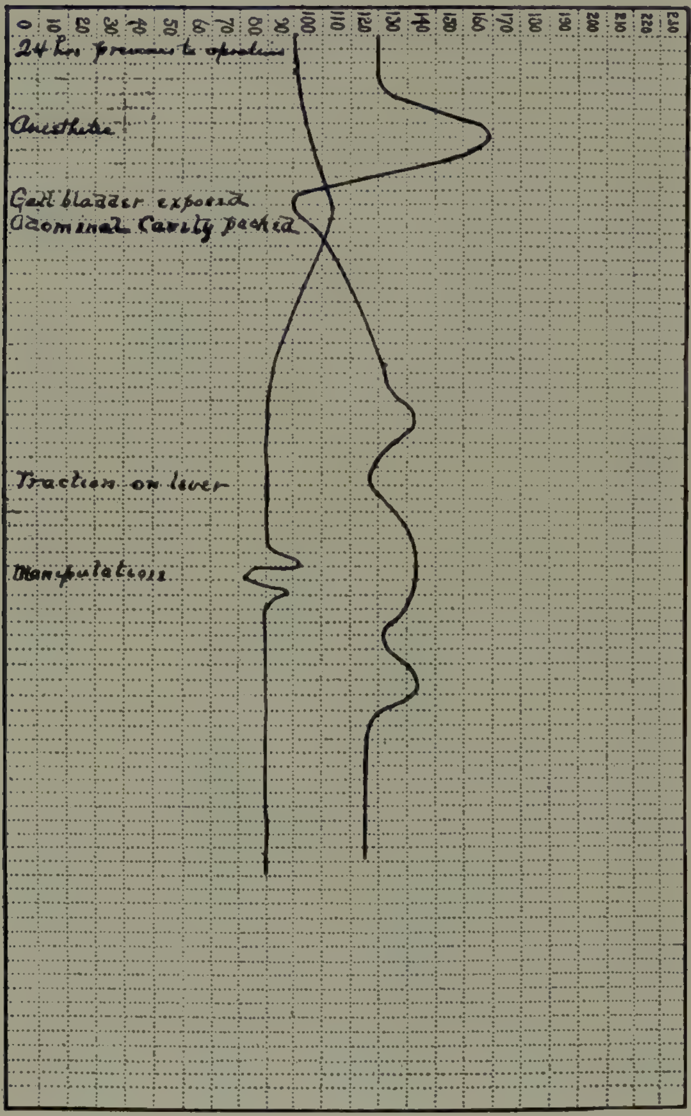

FIG. 22.—OPERATION UPON THE GALL-BLADDER.

Note the marked psychic rise of the blood-pressure during the first stages of anesthesia, then the fall in the pressure during manipulation of the peritoneum. After the gall-bladder was well "packed off" and the exploration and development of the field completed, note the recovery of the blood-pressure. Both the experimental and the clinical evidence point to the importance of minimum manipulation.

Abdomen.—Observations were made during pylorectomy, partial gastrectomy, gastro-enterostomy, choledochotomy, cholecystostomy, cholecystectomy, appendectomy, resection of the cecum, and resection of the large and small intestines. It was found that the amount of shock was directly proportional to the amount of traumatism inflicted upon the peritoneum. The mucous membrane of the hollow viscera did not seem to be capable of producing shock. Exposure to the air, manipulation, and sponging caused a fall in the blood-pressure and a rise in the pulse-rate. This was noted in packing the abdominal cavity with gauze. Flushing out the cavity also caused a decline in the blood-pressure. A most marked effect was noted during the exploration of the abdominal cavity in the development of the field of operation, separating adhesions, and bringing tumors into the wound (Fig. 22).

In operations involving only a small segment of the intestine, although considerable time was occupied, there was little change in the pressure after the first effect had worn off. This was true only when the remainder of the peritoneal cavity was kept free from irritation, as, for example, during the application of the sutures in an anastomosis, but slight change in the blood-pressure was noted. The same is true in appendectomy. During the technic of the appendectomy but little change was noted. In operations such as the dissection of gangrenous bowel in strangulated hernia, the extensive washing and sponging of the field to remove infection was attended by a considerable decline in the blood-pressure. The manipulation which caused the changes in the blood-pressure in almost every instance caused an increase in the respiration.

The Doctors Mayo, of Rochester, Minnesota, from their extensive clinic, made observations upon twenty-five cases of gall-stone operations in which the increase in the respiration and in the pulse-rate was noted. The pulse and the respiration were increased during the manipulation, particularly while removing common duct stones, and in exploration of the field. Observations upon the respirations and the pulse in my own cases of gall-stone operations corroborated these results. The most striking effects were noted in the operations in the upper portion of the peritoneal cavity near the diaphragm. The lower portion of the abdominal cavity showed less reaction. In all the abdominal operations above mentioned the net tendency of the changes was toward decline. In some instances a temporary rise appeared, but this usually gave way to greater decline. In the female genital organs observations were made during operations for resection of the ovaries, the removal of ovarian tumors, excision of the tubes for pyosalpinx, myomectomy, hysterectomy, both abdominal and vaginal, dilating and curetting the uterus, and plastic operations upon the vagina and peritoneum. In almost every instance the immediate effect of manipulation of these organs was a rise in the blood-pressure. This rise usually continued during the period of manipulation, and was proportional to the traumatism administered. The most marked rise was noted in the case of large fibroid tumors, in which considerable difficulty, owing to impaction and adhesion, was experienced in raising the tumor from its bed. Similar results were noted in the different operations upon the perineum and vagina. Divulsion of the sphincter ani caused a very marked rise in the blood-pressure and some increase in the pulse-rate (Fig. 23). The respirations were markedly increased in depth and rhythm. During the manipulation of the sigmoid, respiration was always increased, particularly in its inspiratory phase. This also occurred in dilating the cervix.

Genito-urinary System.—Blood-pressure determinations were made during nephrectomy, nephrotomy, nephrorrhaphy, and suturing of the ureter. During the removal of a large, inflamed carcinoma of the kidney the blood-pressure fell rapidly. In nephrorrhaphy and incising the kidney slight effects were noted.

Testicles.—In dissecting a firmly adhering sac of a scrotal hernia, marked fall in the blood-pressure was noted. In excising the thickened hydrocele sac, the same was noted. In all manipulations, when any effect was noted, it was a fall. In amputation of the penis in an elderly subject the fall was marked (Fig. 24). During careful dissection of the enlarged veins of a varicocele no effect was noted.

Spinal Column.—Blood-pressure determinations in two laminectomies under cocain anesthesia were made. Incising the skin, fascia, muscles, and the bones caused no appreciable change in the pressure. On exposing and exploring the membranes of the cord a marked fall in the blood-pressure occurred.

In one case the exploration extended from the fifth cervical to the axis. It was found that the deep tissues of the back over the middle line have but few sensory nerves. No cocain was required in the division of the deepest fascia, the separation of the deepest muscles, the division of the spinous processes and the laminæ, and in exploration of the dura mater with the exception of the points of exit of the sensory nerve-roots.

The slightest contact with the sensory nerve-root caused an intolerable electric pain. There was quite a tendency to compensation in the blood-pressure following the fall upon opening the canal and making mechanical contact with the dura.

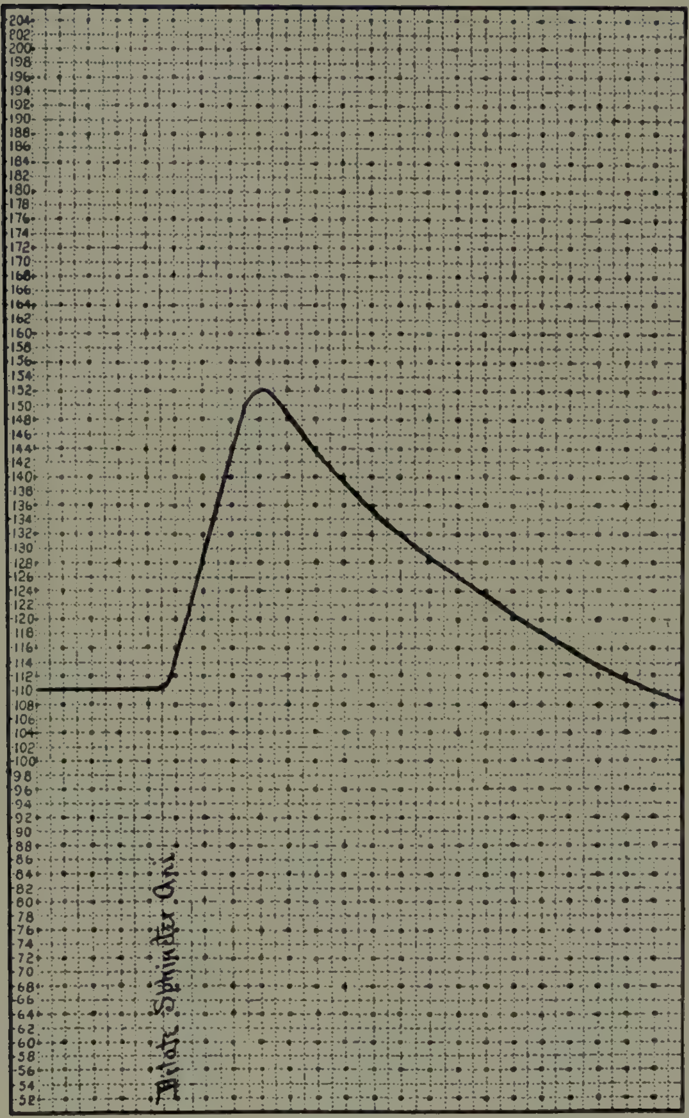

FIG. 23.—DIVULSION OF SPHINCTER ANI.

Note the marked rise in the blood-pressure, corroborating general clinical observation and supporting former experimental evidence.

Hernia.—In operations for inguinal hernia no effect was noted except in those in which there were adhesions of the sac to the spermatic cord, necessitating considerable manipulation. In such cases a fall in pressure was noted. The fall was probably due to the excitation of the characteristic depressor nerve mechanism of the part. In operation for ventral hernia no special changes in the blood-pressure were noted, except in the cases requiring considerable peritoneal manipulation.

Extremities.—Stretching the sciatic nerve caused a marked and irregular rise in blood-pressure and an increase in pulse-rate (Fig. 25). Operating on the soft parts caused an irregularity in the pressure, more particularly a rise. Some of the cases of most profound shock were caused by heavy injuries of the limbs; *e. g.*, railway accidents. In an amputation at the shoulder-joint, in which the trunks of the brachial plexus were cocainized, thereby "blocking" the afferent impulses, no material change in the blood-pressure was noted. In operations upon bone the blood-pressure showed comparatively small variation. The most marked variation was noted during procedure upon the periosteum.

Operations under Cocain.—In abdominal operations under cocain not so much alteration in the blood-pressure was noted as in operations under general anesthesia. This was noted in an operation for typhoid perforation in a boy of twelve years; in a case of cholecystectomy for gall-stones in a woman of seventy; in two cholecystotomies in young adults during typhoid; in a gastrostomy with exploration of the esophagus; in colostomy and other laparotomies. If there was momentary pain or fear the blood-pressure usually rose irregularly. The less amount of shock in these operations under cocain was probably due to several factors. There was no depressing effect of a general anesthetic; the operation did not necessitate much manipulation; and the same precaution against the cause of pain—minimum manipulation—was just as effective

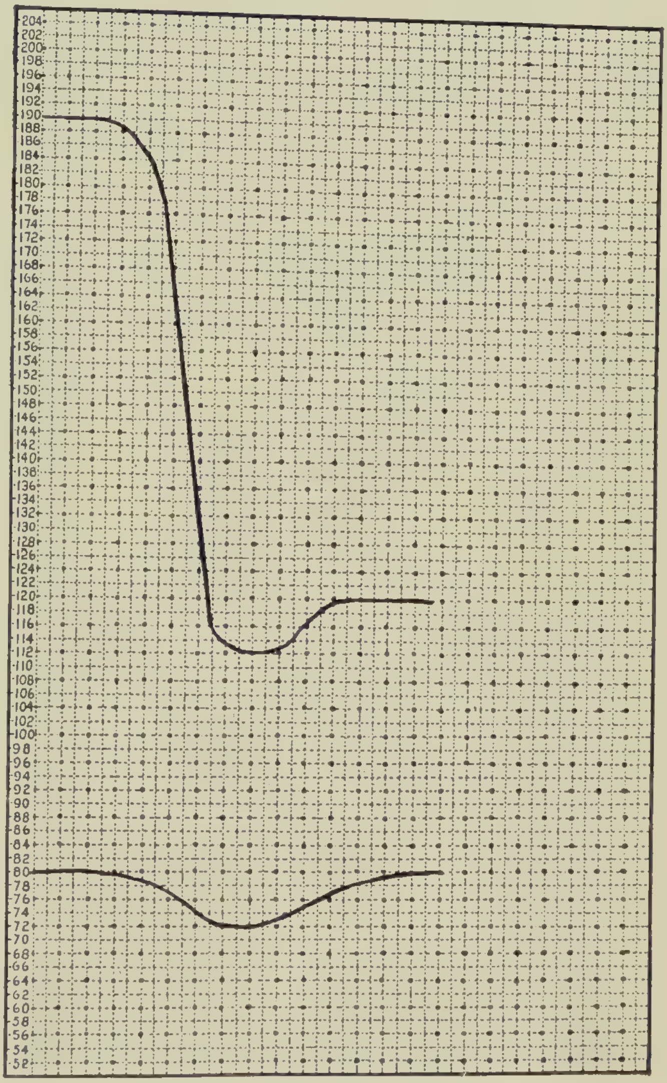

FIG. 24.—PHASE OF AN AMPUTATION OF THE PENIS FOR CARCINOMA IN AN ELDERLY SUBJECT.

Note the striking fall in blood-pressure during the actual amputation. The fall was but temporary. The high initial pressure is commonly found in aged subjects.

against shock. In the instances in which either pain or fear caused a rise in the blood-pressure a later decline was noted. Operations upon the area supplied by nerve-trunks subjected to cocain "block" produced no shock. Interscapulo-thoracic amputations in which the brachial plexus was "blocked" by cocain caused no shock. Collapse in laryngeal and other neck operations may be avoided by the proper use of cocain.

Summary.—The estimations of the blood-pressure by means of a sphygmomanometer were certainly more accurate than the palpation of the radial pulse by the untrained anesthetizer or the inexperienced interne. During important operations and in the after-care of certain cases, blood-pressure determinations were frequently of vital importance. In five cases of typhoid perforations suggestive changes were noted. In one the blood-pressure rose from 90 to 130 mm. in six hours. In a child that was admitted as a case of perforation the blood-pressure was 102 mm. Following the operation for closure of the perforation the general peritonitis disappeared. The pressure then fell to 80 mm. A second perforation occurred on the eighth day. The blood-pressure then rose from 82 to 110 mm. In another case of perforation the blood-pressure was 165 mm. The fifth case registered a pressure of 210 mm. In view of the great variation in individuals, a single observation is of but little diagnostic importance, but repeated observations may have some value. In 115 cases of typhoid the maximum pressure was 138 mm.; the minimum, 70 mm. In the first week the mean pressure was 115 mm.; during the second week, 106 mm.; the third, 104 mm.; the fourth, 96 mm.; the fifth, 98 mm. As opposed to the effect of

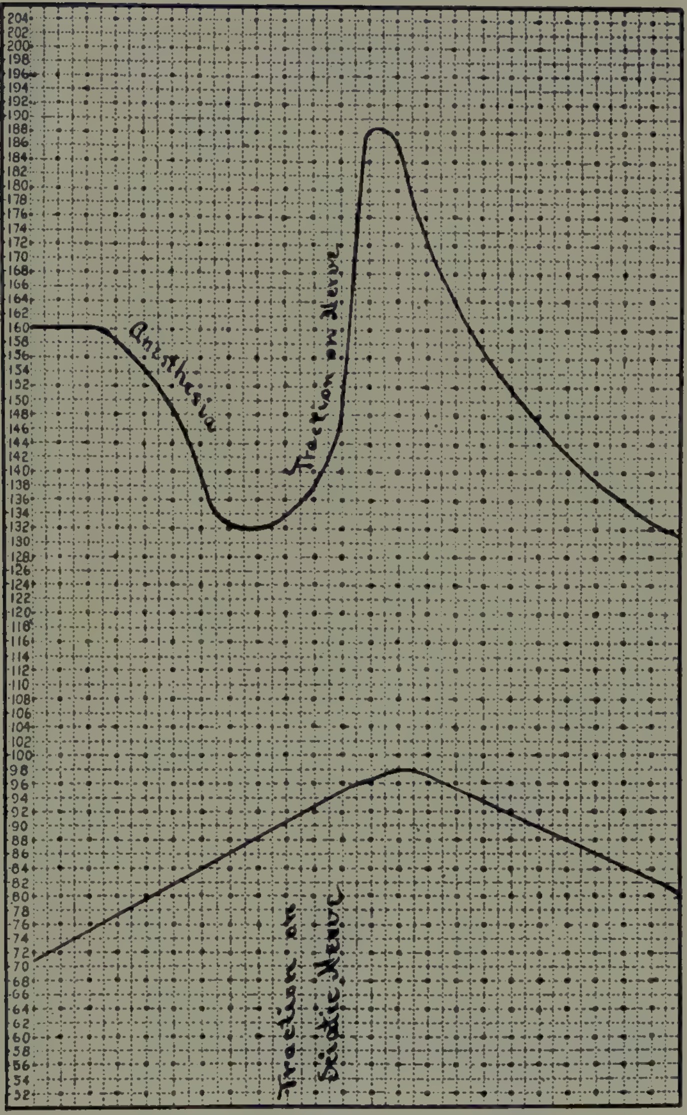

FIG. 25.—STRETCHING THE SCIATIC NERVE FOR INTRACTABLE NEURALGIA.

Note the anesthetic fall (chloroform), then the abrupt rise from 132 mm. to 188 mm. The pulse-rate during the same period rose from 70 to 98. The decline after the stretching was almost as rapid as the rise.

typhoid toxins, acute infective inflammation causes a rise in the blood-pressure. In 23 cases of peritonitis in the height of the attack the minimum pressure noted was 145 mm.; the maximum, 210 mm. The average was 162 mm. Blood-pressure determinations in acute infective inflammations show a rise. These determinations are of but little value in making a prognosis. In the later stages, in the unfavorable cases a rapid fall indicates impending dissolution, but at this stage other symptoms indicate even more clearly the fatal termination.

CHAPTER III.

EXAMINATION OF THE BLOOD.

By John C. Da Costa, Jr., M.D.,
PHILADELPHIA.

I. THE SCOPE OF HEMATOLOGY IN SURGERY.

It is a well-established fact that hematology, if sanely interpreted, is of real value in surgical practice. Weighed as a bit of clinical evidence, the blood report may give either the essential clue to a puzzling group of symptoms, or at least confirm other symptoms and thus complete a picture of disease. But regarded as an infallible sign, affording a specific diagnosis of a given disease, the results of the blood examination are more often misleading than useful. Positive findings with the serum test, with blood culturing, and with search for hemamœbæ settle the diagnosis without further inquiry, as also does the detection of the characteristic leukocyte formula in leukemia and of the distinctive megaloblastic cell changes in pernicious anemia, but these comparatively infrequent findings are of greater interest to the internist than to the surgeon. To the latter the questions of hemoglobin values, the leukocyte count, iodophilia, the coagulation time, bacteriemia, and, perhaps, cryoscopy are important clinical side-lights applicable to routine surgical practice. Negative reports from blood examinations have, at the best, an uncertain value, and, though significant, are not to be depended upon with too much confidence—an abdomen reeking with pus is not invariably incompatible with a normal leukocyte count; failure to culture organisms from the circulating blood by no means rules out sepsis. "Correlate the blood report with the other clinical symptoms" is the maxim for the surgeon to remember, if he would derive from this method of research reliable information of diagnostic and prognostic application.

In this chapter it will be noted that several conditions not strictly of a surgical nature have been described—enteric fever, the primary anemias, the protozoan infections. This has been done for the sake of differential diagnosis, for who, ignorant of their different blood pictures, can apply hematology to the differentiation of such conditions as typhoid fever, malarial fever, and sepsis, cancer and pernicious anemia, leukemia and sarcoma of the spleen, and numerous other diseases having different blood formulas? The salient principles of blood histology and pathology have also been briefly referred to, as essential to the proper reading of that part of the text relating to surgical hematology. Technical methods of blood examination are not germane to the plan of this chapter, and are therefore omitted.

II. GENERAL PHYSIOLOGY AND PATHOLOGY OF THE BLOOD.

General Composition of the Blood.—Normal human blood is composed of fluid and cellular elements, the former constituting three-fifths and the latter two-fifths of its total volume, which in the adult represents from one-thirtieth to one-sixteenth of the body-weight, according to Haldane and Smith.[5] The blood is alkaline in *reaction*, the normal figures ranging from about 200 to 300 mgm. NaOH, and, according to some investigators, even beyond these limits. Permanent changes in the blood reaction probably do not occur so long as the emunctory organs act adequately. Decreased alkalinity is commonly found in the severe anemias and cachexias, in uremia, diabetes mellitus, and cholemia, in Asiatic cholera, in many of the dermatoses, and after chloroform narcosis. Up to the present time alkalimetry of the blood has been of laboratory rather than of clinical interest. The *specific gravity* of the blood varies from 1.055 to 1.065 in the healthy male adult, but is somewhat lower in the female and in the child. The specific gravity is temporarily increased by factors which tend to inspissate the blood—fasting, diarrhea, sweating, emesis, pyrexia, and cyanosis; it is decreased whenever the blood mass is diluted, as in anemia, after the injection of normal salt solution, and following the ingestion of a large volume of liquid. In a general way the specific gravity corresponds to the richness of the blood in hemoglobin and erythrocytes, but it is not a sure quantitative index to these constituents. Clinically, specific gravity testing is far more complicated and less accurate than hemoglobinometry.

The fluid constituent of the blood, the *plasma* or *liquor sanguinis*, is a clear yellowish fluid, of a specific gravity ranging between 1.026 and 1.030, and containing about 10 per cent. of solids, chiefly proteids. *Serum*, a product of coagulation, is a pale straw-colored fluid, having practically the same density and amount of solids as the plasma, from which it differs chiefly in containing fibrin ferment instead of fibrinogen. The principal *salt* of the blood is sodium chlorid, the others being in the form of sulphates and the salts of potassium, magnesium, and calcium. The *gases* of the blood, of which approximately sixty volumes are contained in each one hundred volumes of the whole blood, are oxygen, carbon dioxid, and nitrogen, the first existing chiefly in the hemoglobin of the erythrocytes, the second occurring as carbonates, and the last being held in simple solution. Among the *extractives* of the blood are urea, cholesterin, creatin, xanthin, sugar, and fats.

The most important *cellular elements* of the blood are the erythrocytes or red corpuscles and the leukocytes or white corpuscles. The blood plaques and the hemokonia may be classed with the blood cells, although these bodies probably are not histologic entities.

Coagulation and Fibrin.—Extravascular coagulation, due to an obscure interaction of fibrinogen, a ferment, and a calcium salt, separates the blood mass into two distinct portions, a gelatinous clot or *crassamentum*, and a fluid, *serum*. The clot consists of a mass of fibrin in the delicate meshes of which the blood cells are imprisoned; the serum is simply blood plasma minus the elements from which the clot-fibrin was evolved. In a vesselful of slowly coagulated blood the clot may show two clean-cut strata—a lower deep red layer of erythrocytes, and an upper yellow-gray zone of leukocytes, which constitutes the *buffy coat* of the clot, so frequently referred to by the older pathologists.

Hematopexis.—The term *hematopexis* has been coined by W. W. Keen to express the coagulation time of the blood. Normal blood coagulates within from three to six minutes after having been shed,* but in a number of pathologic states the coagulation time is either delayed or hastened. Hematopexis is considerably *delayed* in many cases of jaundice, anemia, anasarca, hemoglobinemia, hemophilia, purpura, asphyxia, acute alcoholic poisoning, and other toxic conditions. Marked delay in clotting occurs in poisoning by cobra venom and in mild cases of daboia poisoning, but in an individual inoculated with an excessive amount of the latter venom fatal intravascular clotting may be excited. Hirudin, a leech extract, has a remarkable effect in preventing both intravascular and extravascular coagulation. According to Bodong's experiments,[1] blood once hirudinized never regains its clotting power, and blood beginning to coagulate at once ceases to do so on the addition of hirudin. Permanent fluidity of the blood *in vitro* has also been observed in fatal poisoning by prussic acid.[2]

The coagulation time of the blood in jaundice appears to depend not upon the jaundice *per se*, but rather upon such attendant factors as toxemia, hemoglobinemia, and excessive anemia. Fatal post-operative hemorrhage has occurred in cases of malignant disease of the biliary passages with jaundice, but, on the other hand, in the obstructive jaundice of cholelithiasis this accident seems not to have been encountered. In purpura the clot, though formed, is imperfectly retracted and the serum is proportionately scanty (Sicard[3]). In the early days of an attack of enteric fever an appreciably delayed coagulation may predispose to intestinal hemorrhage, while in the later stages of this infection the clotting time may be so rapid as to favor thrombosis. This tendency to rapid coagulation is believed to be due to the excessive quantity of calcium salts in the blood of the convalescent typhoid, since an unduly large amount of lime salts is necessarily ingested by a patient kept for weeks upon a milk diet. As a preventive of thrombosis Wright and Knapp[4] suggest partial decalcification of the milk, by the addition of sodium citrate, as soon as the danger of intestinal hemorrhage is past.

Coagulation is *accelerated* by the administration of calcium salts in small doses, but if the dose be too large or if its use be continued too long, just the opposite effect is produced. From 60 to 90 grains daily of calcium chlorid for three or four days is the proper treatment to promote clotting in a patient whose coagulation time is delayed. Gelatin acts similarly, but much more feebly and erratically than calcium, for which it is but an indifferent substitute. Aside from its uncertain action, the possibility that tetanus spores may lurk in a gelatin solution should make one hesitate in selecting this substance for hypodermatic use in the treatment of hemorrhage. W. J. Taylor[6] believes that the use of thyroid extract internally promotes coagulation, and that the drug promises to be of great value to the surgeon in combating hemorrhage. While thyroid extract decidedly hastens the clotting of blood whose hematopexis is unduly slow, it appears to have no such effect on blood which coagulates normally. The most certain results are obtained by administering the dried extract, in doses of nine grains daily, for from three to seven days before operation.

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*Here may be noted Wright's statement ("Brit. Med. Jour.," 1902, ii, 1706), thus far uncorroborated, that in the healthy male adult clotting may, in the exceptional instance, fail to occur for as much as fifteen minutes.

Hyperinosis, or an increase in the amount and density of the fibrin network, is usually found in acute inflammatory febrile diseases, especially in those accompanied by sero-fibrinous and by purulent exudates. According to Hayem,[7] the density of the fibrin network roughly indicates the degree of the individual's resisting powers against infection. Abscess, pleural effusion, croupous pneumonia, rheumatic fever, peritonitis, erysipelas, variola, and influenza are examples of febrile infections in which hyperinosis occurs. As a rule, hyperinosis and inflammatory leukocytosis (*q. v.*) coexist, though exceptions are to be found in malignant disease and in purpura, in which conditions leukocytosis unattended by a fibrin increase is commonly detected; in influenza, on the contrary, there is a normal leukocyte count with decided hyperinosis. That all febrile states do not imply a fibrin increase is shown by the normal condition of the fibrin, if not, indeed, by the hypinosis, occurring in the pyrexias of grave primary anemias.

Hypinosis means a deficiency in the quantity of fibrin. Fibrin is not increased in malignant disease, tuberculosis, the malarial fevers, enteric fever, purpura, and the primary anemias, and occasionally a decided hypinosis occurs in these conditions.

The Freezing-point of the Blood.—Cryoscopy, or the process of estimating the freezing-point of liquids, has been applied to the blood and urine, with the object of determining their molecular concentration. Surgically, cryoscopy has been used chiefly in gaging the integrity of the kidneys. The freezing-point (expressed by the symbol △) of normal blood ranges between —0.56° and —0.58° C., while normal urine freezes between —0.9° and —2° C. Korányi's pioneer work[8] showed that in diseases of the kidneys involving renal insufficiency the △ of the blood falls and that of the urine correspondingly rises, these changes being due to the surcharging of the blood with excrementitious matter which the crippled kidneys fail to discharge. Single nephrectomy, he found, does not affect the normal △ of the blood and urine, but double nephrectomy lowers the △ of the former and raises the △ of the latter. Kümmel,[9] and later Rumpel,[10] Lindeman,[11] and others, are responsible for the current impression that nephrectomy is contraindicated when the △ of the blood is —0.6° C. or lower and the △ of the urine is 1° C. or higher, the presumption being that when these figures are attained both kidneys are implicated too extensively to insure adequate elimination if one kidney is removed. That this impression needs revision has been shown recently by Loeb and Adrian[12] and by Rovsing,[13] who find that unilateral renal lesions may cause decided abnormalities of the △, while, on the other hand, bilateral disease may exist with no such changes. It is of clinical interest to know that the △ of blood rises in uremia, nephritis, pneumonia, hemoglobinemia, cyanosis, and high-grade anemia. Cystitis and pyelitis do not alter the blood's △.

Since the molecular concentration of the blood may be exaggerated by circulatory stasis, dependent upon cardio-vascular and hepatic diseases, abdominal neoplasms and like factors, all such causes of vascular embarrassment must be excluded before interpreting the findings of the cryoscope. Any departure from the normal should compel a careful revision of all the symptoms before deciding upon surgical interference, but cryoscopy alone is of doubtful value in determining the state of renal activity; it can afford no certain clue to the compensatory hypertrophy which a kidney may undergo. This question, together with other clinical features of cryoscopy, has been ably treated by Casper and Richter,[14] by Tinker,[15] and by Ogston.[16]

Hemoglobin.—Hemoglobin occurs in the stroma of the erythrocytes as oxyhemoglobin, an albuminous and ferruginous substance readily yielding oxygen to the tissues and highly susceptible to union with various gases, such as carbon monoxid and carbon dioxid. Hemoglobin is derived chiefly from the iron ingested in the form of food; but should this source of supply be cut off, it may be formed from the iron stored up in the liver and other organs. Iron is the most useful blood-builder for patients deficient in hemoglobin; arsenic, though it indirectly stimulates hemogenesis, has little or no effect in exciting a hemoglobin increase. (Aporti;[17] Bergmann;[18] Baumann.[19])

The *absolute amount* of hemoglobin is about 14 grams in each 100 grams of blood, this figure corresponding to the normal percentage of hemoglobin, arbitrarily fixed at 100. The term *color index* (valeur globulaire; blood quotient) means the proportionate amount of hemoglobin in each erythrocyte, the normal standard, calculated by dividing the hemoglobin percentage by that of the erythrocytes, being 1.00. If, as is commonly the case in chlorosis, the hemoglobin loss greatly exceeds that of the cells, the color index falls decidedly below normal—to 0.50 or lower; if, as is the rule in pernicious anemia, the cellular deficiency greatly outstrips the hemoglobin loss, the color index rises above normal—to 1.25 or perhaps higher; and if, as in the average case of secondary anemia, the hemoglobin and cellular losses are roughly proportionate, the color index deviates but slightly from the normal figure.

Oligochromemia, or diminution in the percentage of hemoglobin, is a blood finding common to all anemic states, and is associated usually with a more or less conspicuous decrease in the number of erythrocytes. Strikingly low hemoglobin percentages are found in chlorosis, in pernicious anemia, and in the anemias secondary to hemorrhage, sepsis, and malignant disease. These average findings in 150 consecutive cases of anemia illustrate the differences in the hemoglobin content in anemias of different origin:

Pernicious Anemia:	average loss in 50 cases....	74.5 per cent.
Chlorosis:	" " " " "	56.8 " "
Secondary Anemia:	" " " " "	44.8 " "

The symptomatic anemias attending the chronic constitutional diseases, the infections, the hemorrhagic disorders, and the various toxic states also involve considerable diminution in the hemoglobin.

Moderate oligochromemia develops after anesthesia by ether and by chloroform, the loss generally being more pronounced the lower the pre-anesthetic hemoglobin figure. This fact accounts for the prevalent belief, popularized by Bierfreund,[20] that a hemoglobin percentage below 30 or 40 contraindicates general anesthesia. In cases of imperative necessity this arbitrary rule, of course, must be disregarded, but in other instances it is wiser to postpone the anesthesia until the hemoglobin loss has been restored by the use of iron, or to substitute a local for a general anesthetic. That Bierfreund's dictum is by no means invariably true is shown by the numerous reports of successful operations under general anesthesia in subjects with hemoglobin percentages ranging between 15 and 30.[21] Hutchins[22] has recently reported 60 operative cases with hemoglobin figures of 50 or less, in none of which did the etherization prolong or unduly aggravate the anemia.

Splenectomy and double oöphorectomy are followed by lower hemoglobin figures than the mere post-operative blood loss appears to warrant. A hemoglobin percentage 10 to 15 points below the normal standard is physiologic in women just before the onset of menstruation, with the full establishment of which this preliminary oligochromemia promptly disappears.

In the interpretation of the hemoglobin value it must be remembered that factors of blood concentration may account for abnormally high figures, while in diluted, hydremic blood the reverse occurs, the gain or loss in either instance paralleling the fluctuations of the erythrocytes. (See "Polycythemia," p. 121.)

Hemoglobinemia, or the presence in the blood plasma of hemoglobin dissolved from the erythrocytes, may be due to actual cellular destruction (hemocytolysis) or to a simple disunion of the hemoglobin and the cellular stroma and its escape from the latter into the plasma. In hemoglobinemia the whole blood loses its normal opacity and becomes decidedly transparent, and the serum is tinged a clear ruby-red color ("laked" blood). Prominent causes of hemoglobinemia, and, in extreme cases, of hemoglobinuria, include sepsis and many of the acute specific infections, various chronic cachexias, the hemorrhagic disorders, Raynaud's disease, and those obscure diseases known as epidemic hemoglobinuria and paroxysmal hemoglobinemia. Insolation, severe burns, extensive frostbite, and the transfusion of alien blood also liberate hemoglobin from the cells. The administration of the so-called "blood-poisons" in toxic amounts (especially the coal-tars, chlorates, iodids, mercury, nitrites, and strong acids) may account for active erythrocyte disintegration and consequent hemoglobinemia, as also may other toxic substances such as snake and scorpion venoms and certain of the vegetable poisons.

Methemoglobinemia is characterized by the presence of methemoglobin in the erythrocytes, this abnormal pigment being a modified form of oxyhemoglobin in which the oxygen is so firmly incorporated with the cells that their oxygenating powers are inhibited. Like hemoglobinemia, methemoglobinemia is produced by poisoning with the coal-tars, iodids, and nitrites, as well as by a number of other less familiar toxic substances. The same change has also been observed in malignant edema, purpura hemorrhagica, and Addison's disease.

Carbon monoxid hemoglobin is a blood change occurring in coal-gas poisoning and in the asphyxia due to the fumes of fire-damp. The change is betrayed by a bright cherry-red color of the blood, both arterial and venous.

Anemia.—The word anemia expresses a deficiency, quantitative, qualitative, or both, in the amount of the blood. A quantitative anemia, or *oligemia,* may exist with no alteration in the composition of the several constituents of the blood, although it generally involves a diminution in the cells and in the solids of the plasma. The best surgical illustration of a quantitative anemia is the deficiency in the volume of the blood immediately after an extensive traumatic hemorrhage. *Ischemia* is a local anemia, due to interference with the blood-supply of a circumscribed area of the body. A dilution of the blood, relatively increasing its liquid elements, constitutes *hydremia,* this change being common to the various anemias, and occurring also as the result of dropsy, of extreme vasomotor dilatation, and of the ingestion or the injection of large quantities of fluids. *Anhydremia,* or an inspissation of the blood, is characterized by a relative diminution in the liquids, this change being due to drains upon the body-fluids (diarrhea, urinary crises, emesis, sweating, and effusions) and, to a moderate degree, to increased arterial tension. *Pseudoanemia* is a spurious anemia, in which the objective signs of anemia exist and yet examination shows a normal blood picture. This apparent blood deterioration is best explained by such factors as hereditary peculiarities, vasomotor disturbances, and anomalies of the pigment and the capillary network of the skin. The "prison bleach" of the convict and the peculiar pallor of the resident in the tropics do not necessarily signify an actual blood poverty.

Owing to our uncertain knowledge of blood pathology, it is necessary arbitrarily to classify all forms of anemia as *primary* or *essential,* and as *secondary* or *symptomatic.* The primary anemias are those in which the etiology is either obscure or insufficient to account for the blood changes, which are attributed to grave lesions of the blood-making organs, this group including chlorosis, pernicious anemia, lymphatic and myelogenous leukemia, Hodgkin's disease, and perhaps splenic anemia. The secondary anemias comprise those with a perfectly clear etiology and without essential involvement of the blood-making apparatus. They include the anemias secondary to hemorrhage, inanition, faulty hygiene, intestinal parasites, metal poisoning, acute infections, and the cachexias incident to many chronic diseases. To the surgeon the anemias of greatest practical interest are those secondary to hemorrhage, suppuration, sepsis, and malignant disease.

Primary Anemia.—*Chlorosis.*—This disease is characterized by a hemoglobin loss greatly disproportionate to that of the erythrocytes, and therefore productive of a low color index, since the cells individually are deficient in their hemoglobin content. The erythrocytes are generally decreased in diameter, but they rarely show marked structural degeneration, and erythroblasts, save for an occasional normoblast in severe cases, are not found. The number of leukocytes is not increased, but a relative lymphocytosis and a subnormal number of eosinophiles are common findings. Other changes include an increase in the volume of the plasma with a diminution in the oxygen capacity of the blood unit (Lorrain Smith,[23] Lloyd Jones[24]), and a striking deficiency in the quantity of blood albumin (Biernacki[25]). Since several other conditions (notably syphilis, tuberculosis, and chronic nephritis) may provoke a so-called "chlorotic" state of the blood, hematology must be supplemented by other clinical methods in the diagnosis of chlorosis.

Pernicious Anemia.—The erythrocyte decrease is strikingly disproportionate to the hemoglobin loss, so that a high color index is the rule, owing to a relative excess of hemoglobin in the individual cells. The erythrocytes are much distorted, show granular degeneration, and are generally increased in diameter. In typical cases there are numerous megaloblasts and normoblasts, the former type of cells predominating—the so-called "megaloblastic blood picture." The number of leukocytes is either normal or subnormal, and a relative lymphocytosis, together with the presence of a few myelocytes, can usually be detected. The blood volume fluctuates in different cases, but a true general increase is unlikely. The total oxygen capacity of the blood is greatly diminished (Lorrain Smith[26]). The albumin content of the whole blood is decidedly subnormal (Gumprecht and Stintzing[27]), although the serum albumin is but moderately reduced (Diabella[28]). Pernicious anemia differs from *chlorosis* and from *secondary anemia* in having a high color index, a prevalence of megalocytes and megaloblasts, and a decided leukopenia with relative lymphocytosis. The anemia of *Bothriocephalus latus* infection, which may precisely simulate pernicious anemia, promptly disappears after the expulsion of the parasites from the gut.

Leukemia.—In *lymphatic leukemia* the typical blood picture is one of lymphemia, or an absolute and a relative increase in the number of lymphocytes, these cells ordinarily constituting more than nine-tenths of the total leukocyte count, which may be twenty or thirty times in excess of the maximum normal standard. As a general rule, the more acute the case, the greater the tendency toward a large-celled lymphocytosis. Well-marked hemoglobin and erythrocyte losses, with correspondingly severe degenerative cellular changes, are also conspicuous. In *myelogenous leukemia* the characteristic blood change is known as myelemia, that is, the presence of large numbers of myelocytes in the circulating blood. This type of marrow cell constitutes about one-fifth of the total leukocyte count, which is ordinarily forty or fifty times higher than normal. Mast cells are also very numerous, and the eosinophiles are increased. The hemoglobin and erythrocytes are diminished, and the cellular degeneration is usually of high grade; nucleated erythrocytes, the majority of which are normoblasts, are commonly found in large numbers. An *intercurrent infection* developing in a leukemic subject usually excites prompt and striking changes in the leukocytes, as well as in the other clinical manifestations of the disease. Generally the leukocytes rapidly fall toward the normal, both quantitatively and qualitatively; sometimes the leukemic blood picture is exaggerated; and exceptionally little or no change takes place. In the first class of cases the fall of the leukocytes is accompanied by a marked improvement in the other symptoms, but with recovery from the complicating disease the blood resumes its leukemic hall-mark and the other evidences of leukemia return. Sepsis, pneumonia, erysipelas, acute tuberculosis, and malignant disease are typical examples of infections acting in this manner, for the details of which Dock's careful résumé [29] should be consulted.

In contrast to lymphatic leukemia, the blood of the myelogenous variety shows a more moderate type of anemia but a greater number of normoblasts, and a much higher count of leukocytes, among which myelocytes, eosinophiles, and mast cells are conspicuous. In a high leukocytosis the *number* of leukocytes may be as great as in leukemia, but the polynuclear neutrophiles (not the lymphocytes nor the myelocytes) are the cells responsible for the increase. An *absolute lymphocytosis* (such as may occur in pertussis, in infantile pneumonia, or in lymphosarcoma), by involving a high absolute and relative lymphocyte increase, may resemble lymphatic leukemia; in this sort of lymphocytosis, however, the increase is moderate and temporary, the anemia is not usually marked, and the etiologic factors are sufficiently conclusive. *Chloroma, multiple periostitis,* and *Still's disease* all are clinically not unlike leukemia; in the first-named disease the differentiation must often be made by the objective symptoms, since the blood changes may resemble those of lymphatic leukemia; in the second, which, hematologically, counterfeits myelogenous leukemia, the distinctive history is the clue; and in the third, which, objectively, apes myelogenous leukemia, there is an aleukemic blood picture. The aleukemic state of the blood in cases of *lymphatic hyperplasia* and of *splenic* and *renal tumors* is a sure criterion in distinguishing such lesions from leukemia.

Here may be mentioned the remarkable effect of the Röntgen-ray in the treatment of myelogenous leukemia. The disappearance of the myelemia and of the splenomegaly thus effected is, unfortunately, believed to mirror a symptomatic improvement and not a radical cure of the disease. I have found that röntgenization of the tibial and femoral marrow produces much more rapid and certain results than the exposure of the splenic area to the rays, as is ordinarily practised. Energetic treatment with arsenic alone sometimes causes similar results. The reader should consult Dock's monograph [30] and the articles by Brown and Jack [31] and by Heineke [32] for full data concerning this subject.

Hodgkin's Disease.—Here the blood shows merely a variable grade of anemia, with a normal leukocyte count, or, very rarely, a moderate leukocytosis. These negative findings distinguish Hodgkin's disease from *leukemia,* its clinical counterfeit, but they are no criterion in differentiating other forms of adenoid overgrowth which may be accompanied by identical blood changes.

Splenic Anemia.—Well-defined anemia with leukopenia and relative lymphocytosis is the quite uncharacteristic blood finding in this uncertain clinical entity. Of the several conditions which may be confused with splenic anemia, *myelogenous leukemia* is distinguished by its distinctive myelemia; *pernicious anemia*, by its megaloblastic blood picture; *ague cake*, by the presence of the malarial parasite, or, at least, of pigment; *echinococcus* of the spleen, by eosinophilia; and *malignant disease* of the spleen, by leukocytosis.

Secondary Anemia.—The degree of a symptomatic anemia ranges from a trivial hemoglobin deficiency to a grade of blood impoverishment so striking as to masquerade as true pernicious anemia. The average case, however, shows a well-marked though not excessive hemoglobin and erythrocyte loss, with corresponding evidences of cellular degeneration. The color index is more likely to be moderately subnormal than either extremely high or low. Nucleated erythrocytes, especially normoblasts, occur in severe cases. Moderate leukocytosis, usually due to complications, is found in many instances, and the plaques are generally more numerous than in normal blood.

The following data, based upon 200 consecutive blood examinations, show the average blood changes in different anemias:

FORM OF ANEMIA.	HEMOGLOBIN LOSS.	ERYTHROCYTE LOSS.
Secondary Anemia	44.8 per cent.	27.1 per cent.
Chlorosis	54.8 " "	17.8 " "
Pernicious Anemia	74.5 " "	76.9 " "
Leukemia	60.6 " "	45.4 " "

The special features of the blood in the secondary anemias and the clinical applications of such findings are discussed in Part IV. (See p. 131, *et seq.*)

Alterations in the Blood Volume.—*True plethora* is an increase, cellular and fluid, in the volume of the blood, such as may result temporarily from the transfusion of blood or from forcing into the general circulation the blood of a part to be severed from the body, as by the use of an Esmarch bandage before an amputation. The habitual polyemia of the so-called "plethoric" individual is but conjectural. *Serous plethora* is an increase in the blood volume due to an excess of plasma, attributable to such causes as low vasomotor tension, cardiac failure, and the introduction of an undue amount of fluid by ingestion or by injection. *Cellular plethora*, or polycythemia, is characterized by an increase in the hemoglobin percentage and in the erythrocyte count in excess of the normal standard; it is a relative rather than an absolute condition. (See p. 121.) *Hydremia*, or dilution of the blood, involves simply a relative plasma increase without an increase in the total volume of blood; it may arise from the causes of serous plethora, and also occurs in anemia, in dropsy, and after hemorrhage. *Anhydremia* is a concentration of the blood, dependent upon a loss of plasma, of which change increased arterial tension and sudden, large drains upon the body-fluids are active factors. Dilution and concentration of the blood are of practical interest in the interpretation of the blood report, since in the former condition perfectly normal blood may appear anemic, while in the latter anemic blood may seem normal.

Lipemia.—When the blood contains fat in excess (3.25 parts per thousand being the maximum normal amount), the condition is known as *lipemia*. Physiologically, lipemia occurs during digestion, in the nursling, in obesity, in pregnancy, and as the result of menstrual suppression. Pathologically, it is found in a great variety of lesions, of which the most important are diabetes mellitus, gout, arteriosclerosis, and many of the acute fevers. Fractures involving injury of the fatty marrow and lacerated wounds of blood-vessels traversing fatty tissues also may excite lipemia, which occasionally is so excessive that fatal fat embolism results.[33] *Lipacidemia*, or the presence of volatile fatty acids in the blood, has been noted in diabetes mellitus, in leukemia, and in various pyrexias; in fevers the blood may also contain an appreciable amount of acetone —*acetonemia*.

Glycemia.—When the normal sugar content of the blood, 1 to 1.5 pro mille, is exceeded, the condition is termed *hyperglycemia*. This change is encountered in diabetes mellitus, in carcinoma, in some of the acute infections, after splenectomy, and after ligation of the pancreatic duct. The presence of hyperglycemia in carcinoma and its absence in sarcoma have been emphasized by Freund[34] and by Trinkler[35] as a differential point between these two forms of neoplasm. *Williamson's test*,[36] which consists in the decolorization of an alkaline solution of methylene-blue by diabetic blood, has proved dependable in my hands. *Bremer's test*,[37] or the atypical staining affinities of diabetic blood, is not specific, since similar peculiarities have been noted in non-diabetic bloods.

Other pathologic changes affecting the whole blood include *cholemia*, or the impregnation of the blood with bile or bile pigments which occurs in conditions of icterus; *uricacidemia*, or the presence in the blood of a demonstrable quantity of uric acid, as in gout, leukemia, pneumonia, and a number of other diseases; and *melanemia*, or the occurrence of pigment in the blood—a familiar finding in the malarial fevers, and an occasional one in melanotic sarcoma, in Addison's disease, and in insolation.

Parasitology of the Blood.—**Bacteriemia.**—The demonstration that most of the specific infections are in reality bacteriemias is due to the recent perfection of the technic of blood culturing, a method of research which today furnishes accurate, final information in many obscure diseases. The bacillus of Eberth, for instance, can be cultivated from the blood in about 80 per cent. of all cases of *enteric fever*, the highest percentage of positive findings occurring during the first week of the infection, generally before the appearance of the serum reaction. In *paratyphoid fever* similar results with the paratyphoid organism have also been obtained. In the identification of many puzzling septic conditions bacteriologic examination of the blood frequently gives just the sought-for clue; this is conspicuously true of *malignant endocarditis*, *pneumococcus infection*, *gonorrheal sepsis*, *bubonic plague*, *acute tuberculosis*, *glanders*, *cerebrospinal fever*, and *septic states* of cryptogenic character. The presence of streptococci in the blood in many cases of *scarlatina* and of *rheumatic fever* has also been reported. In *anthrax*, *influenza*, and *Malta fever* the specific bacteria are found in the circulating blood only in exceptional instances.

Hematozoa.—Microscopic examination of the fresh and stained film of finger-blood is resorted to in seaching for the *Hæmamœba malariæ*, the *Spirillum Obermeieri*, the *Filaria sanguinis hominis*, the *Trypanosoma gambiense*, and the *Treponema pallidum*. The *Leishman-Donovan body* of tropical splenomegaly is usually obtained by splenic puncture, since it appears in the general circulation only in rare instances. It may here be noted that the specificity of the so-called *Piroplasma hominis* of Montana spotted fever has not been conclusively proved.

Other blood parasites, not invading the general blood-stream, are the *Bilharzia hematobia*, residing in the portal vein and its branches, and, very rarely, in the pulmonary circulation; and the newly discovered fluke, the *Schistoma cattoi*, inhabiting the capillaries of the intestines, the liver, and other parts of the alimentary canal.

III. THE CELLULAR ELEMENTS OF THE BLOOD.

The Erythrocytes.—The *erythrocytes* or *red corpuscles* are smooth, elastic, non-nucleated biconcave discs, about 7.5 μ* in diameter, and consisting of a spongy network (*the stroma of Rollet*) in the meshes of which the hemoglobin is embedded. In normal blood the erythrocytes tend to collect and adhere like rolls of coins stacked up face to face, this being known as *rouleaux formation*. A loss of this tendency (*hypoviscosity*) occurs in severe anemia, and an exaggeration of the cells' adhesive properties (*hyperviscosity*) is met with in many of the acute infections and as the result of the toxic action of certain blood poisons.

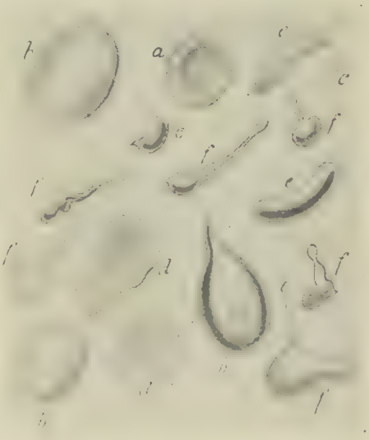

FIG. 26.—DEFORMITIES OF SIZE AND SHAPE OF THE ERYTHROCYTES.

a, Normal erythrocyte; *b*, megalocytes; *c*, microcytes; *d*, hemoglobin-deficient erythrocytes; *e*, sausage-shaped poikilocytes; *f*, common types of poikilocytes.

The *normal number* of erythrocytes is approximately 5,000,000 per cubic millimeter in the man; 4,500,000 in the woman; and from 6,000,000 to 7,000,000 in the newly born infant. The *volume index*, indicating the percentage volume of the individual cell, is normally 1.00; it roughly parallels the color-index, falling notably in chlorosis, declining moderately in leukemia and in the secondary anemias, and rising above normal in true pernicious anemia. *Polycythemia*, or an increase in the number of erythrocytes above the normal standard, may be due to physiologic and to pathologic factors. Physiologically, an increase of this sort occurs during digestion, and from the effects of active muscular exercise, massage, cold or hot tubbing, and fasting. Normal pregnancy, lactation, and menstruation cause little or no numerical changes in the cells. Pathologically, polycythemia is referable to many different causes, mainly those which concentrate the blood either by draining off its liquids or by provoking peripheral stasis. Thus, abnormally high erythrocyte counts develop during residence in high altitudes; as the result of active purging, emesis, and sweating; during the reformation of an exudate following paracentesis; from the effects of cyanosis, as in Osler's disease, valvular cardiac lesions, pulmonary diseases, and asphyxia; and after blood transfusion and during active hemogenesis. The number of cells is also greater than normal in many cases of incipient phthisis, acute yellow atrophy of the liver, myxedema, diabetes mellitus, bubonic plague, severe burns, insolation, and poisoning by phosphorus and by illuminating gas.

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*The Greek μ (micromillimeter) stands for $\frac{1}{1000}$ mm. in microscopy.

Oligocythemia, or a diminution in the number of erythrocytes, is symptomatic of some form of anemia, and is accompanied by more or less hemoglobin loss or oligochromemia, and perhaps occasionally by a reduction in the blood volume or oligemia.

Pathologic Structural Changes.—*Deformities of Size and Shape.*—Changes affecting the size and the shape of the erythrocytes occur in all severe anemias, the degree of such alterations corresponding to the grade of the anemia of which they are symptomatic. These abnormalities are due to some form of defective hemogenesis, owing to which faultily formed and peculiarly vulnerable cells are bred in the bone-marrow, and thence reach the general circulation. Abnormally large-sized cells are known as *megalocytes* (Fig. 26), and the prevalence of such cells (*megalocytosis*) is the rule in severe types of anemia, especially in the pernicious form, of which a general increase in the erythrocytes' diameter is a clinical hallmark. Unduly small-sized erythrocytes are termed *microcytes* (Fig. 26), and their presence in large numbers (*microcytosis*) is a common finding in chlorosis and in well-marked secondary forms of anemia. *Poikilocytes* (Fig. 26) are misshapen erythrocytes of various sizes and of differing grades of deformity; such cells, while not distinctive of any specific kind of anemia, are especially numerous (*poikilocytosis*) in pernicious anemia and in leukemia. The above varieties of cell deformity generally coexist in conditions of blood impoverishment, and the general rule holds true that the milder anemias cause moderate microcytosis and small-celled poikilocytosis, and that the severer forms excite extreme megalocytosis and large-celled poikilocytosis.

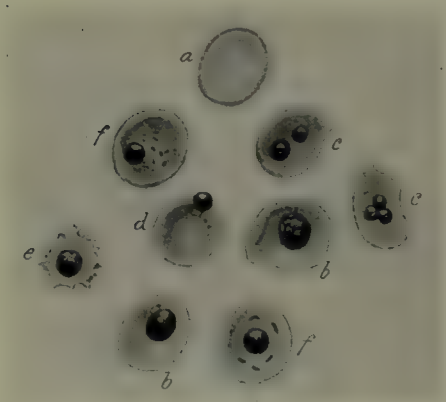


Fig. 27.—Types of the Normoblast.

a, Normal erythrocyte; *b*, common types of the normoblast; *c*, normoblasts containing multiple (divided) nuclei; *d*, normoblast showing apparent nuclear extrusion; *e*, microblast; *f*, normoblasts showing granular basophilia.

The foregoing changes are closely associated with *endoglobular necrosis* of the cells which results in their dehemoglobinization, and with *total cell necrosis,* which is an extreme type of structural decay ending in fragmentation or *schistocytosis.*

Erythroblasts.—Nucleated erythrocytes or erythroblasts are of two distinct varieties, normoblasts and megaloblasts, each of which differs not only histologically, but also in origin and in clinical significance. The typical *normoblast* (Plate I; also Fig. 27) is a cell the size of the normal erythrocyte (normocyte), and is provided with a relatively small spherical nucleus which stains deeply with the basic anilin dyes; in some forms the nucleus is apparently extruded from the cell-body, in others it is convoluted or actually divided, and in still others it is of large size and of a feebly basic tendency, these last peculiarities betraying extreme histologic youth. The cell-stroma usually resembles that of the normocyte. The *megaloblast* (Plate I; also Fig. 28) is a large-sized cell, and its nucleus, which is very feebly basic, occupies the greater part of the cell-body; in atypical forms the nucleus is twisted, indented, or divided, and deeply stained, this peculiarity being a sign of extreme senility. The cell-body is often swollen, irregular, and marked by stigmata of degeneration. (See below.) The *microblast* is a small nucleated erythrocyte, consisting of a spherical basic nucleus encircled by a narrow ragged rim of cell-body. This cell is regarded as a normoblast dwarfed by the degeneration and solution of its protoplasm.

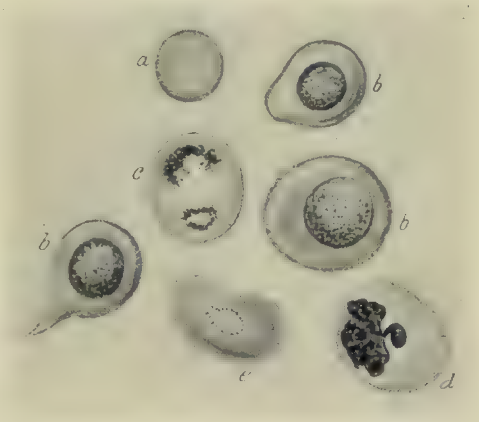


FIG. 28.—TYPES OF THE MEGALOBLAST.
a, Normal erythrocyte; *b*, common types of the megaloblast; *c*, megaloblast showing nuclear division (karyokinesis); *d*, megaloblast showing nuclear solution (karyolysis); *e*, erythrocyte containing a ring body.

The presence in the blood of any form of nucleated erythrocyte indicates an intense anemia, and the adequacy of the bone-marrow in compensating the blood loss is shown by the prevailing type of such cells. Normoblasts, bred in normal marrow, stand for active, adult hemogenesis, and are the prevailing erythroblast found in anemias with active regeneration of the blood, such as chlorosis, post-hemorrhagic and other favorable secondary anemias; megaloblasts, originating in fetal marrow, betray sluggish, embryonic hemogenesis, and are the predominating nucleated cell in pernicious anemia, in which embryonic reversion of the marrow exists. The gravity, then, of an anemia is reflected by the relative abundance of these two opposite types of erythroblasts, since the normoblast expresses regeneration, and the megaloblast degeneration, of the hematopoietic functions.

Polychromatophilia and Granular Basophilia.—The normal erythrocyte, when stained with a mixture of acid and basic dyes, shows a selective affinity for the acid dye, but the pathologic erythrocyte loses this affinity and is stained irregularly by both acid and basic elements, thus exhibiting *polychromatophilia* or *anemic degeneration*, a change whose intensity is gaged by the cell's capacity for the basic stain. Polychromatophilia is distinctive of no special type of anemia, but it is particularly well marked in pernicious anemia and in the leukemias. *Granular basophilia* is a peculiar basic stippling, fine or coarse, of the stroma of the erythrocyte, best brought out with eosin-methylene-blue mixtures. It is probably a sign of stroma degeneration, affects both erythrocytes and erythroblasts, and is frequently associated with polychromatophilia. Basophilic cells may be found in many forms of severe anemia, but they are especially common in lead poisoning, in pernicious anemia and leukemia, and in the anemias secondary to sepsis, malignant disease, and the acute infections.

Ring Bodies.—Ring-shaped bodies within the erythrocytes and similar extracellular figures, staining both metachromatically and basically, have been described by Cabot[38] and by Strauss and Rohnstein.[39] They closely resemble the nuclear outlines of erythroblasts and suggest nuclear remnants. Cabot has found such ring-bodies in lead poisoning, in leukemia, and in pernicious anemia, and I have also noted them in the latter disease, as well as in the anemia of grave sepsis. A special form of stroma degeneration known as *Schüffner's granules* is met with in tertian malarial fever, and consists of a coarse red stippling of the parasitiferous erythrocytes in specimens stained with polychrome methylene-blue.

The Leukocytes.—The *leukocytes* or *white corpuscles* are nucleated colorless cells, most of which are of larger size than the erythrocytes, by which they are outnumbered approximately seven-hundredfold. They appear as irregular spheroidal bodies consisting of a nuclear mass and a protoplasmic body which in some of the cells is quite hyaline and in others crowded with delicate granules. In the adult the *normal number* of leukocytes ranges between 5,000 and 10,000 per cubic millimeter of blood, and averages about 7,500; in the young infant a count of 20,000 or 30,000 is physiologic. Details relating to phagocytosis, pinocytosis, opsonic action, and other phases of the leukocyte function are dealt with elsewhere. (See p. 174.)

Varieties of Leukocytes.—The different varieties of leukocytes are identified microscopically both by their morphology and by the technic of "color analysis," first proposed by Ehrlich.[40] By this method the various structures of the cells—nucleus, protoplasm, and granules—are selectively colored by staining a dry, fixed blood film with the acid, basic, and neutral anilin dyes, so that their distinctive characteristics may be readily distinguished. In a specimen of normal blood thus stained the following types of leukocytes are demonstrable:

VARIETY OF CELL.	RELATIVE PERCENTAGE.	ABSOLUTE NUMBER PER CUBIC MILLIMETER OF BLOOD.
Small lymphocytes	20 to 30	1,000 to 3,000
Large lymphocytes and transitional forms	4 to 8	200 to 800
Polynuclear neutrophiles	60 to 75	3,000 to 7,500
Eosinophiles	.5 to 5	25 to 500
Basophiles	.5	25

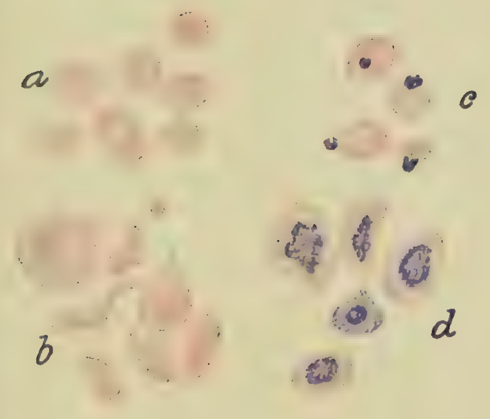
In addition to these six normal varieties of leukocytes, there are three pathologic types which are found in the blood only as the result of some hematopoietic disturbance. These cells are the *myelocytes*, the *mast cells*, and the so-called *stimulation forms*.

PLATE I.

NORMAL AND PATHOLOGIC FORMS OF BLOOD-CORPUSCLES.

1. NORMAL, DEFORMED, AND NUCLEATED ERYTHROCYTES. (Wright's Stain.)
    a, Normal erythrocytes; *b*, Deformities of size and shape; *c*, Normoblasts; *d*, Megaloblasts.
2. GRANULAR BASOPHILIA AND POLYCHROMATOPHILIA OF THE ERYTHROCYTES. (Wright's Stain.)
    a, Normal erythrocytes; *b*, Granular basophilia; *c*, Polychromatophilia.
3. NORMAL AND PATHOLOGIC TYPES OF LEUKOCYTES. (Wright's Stain.)
    a, Small lymphocytes; *b*, Large lymphocytes; *c*, Transitional form; *d*, Polynuclear neutrophiles; *e*, Polynuclear eosinophiles; *f*, Eosinophilic myelocyte; *g*, Mast cells; *h*, Neutrophilic myelocytes; *i*, Blood plaques.
4. IODOPHILIA. (Goldburger-Weiss Stain.)
    A. NORMAL BLOOD.
    B. BLOOD FROM A CASE OF SEPSIS.
    a, Granular type of reaction (intracellular); *b*, Diffuse type of reaction (intracellular); *c*, Extracellular iodophilic mass.

PLATE I.



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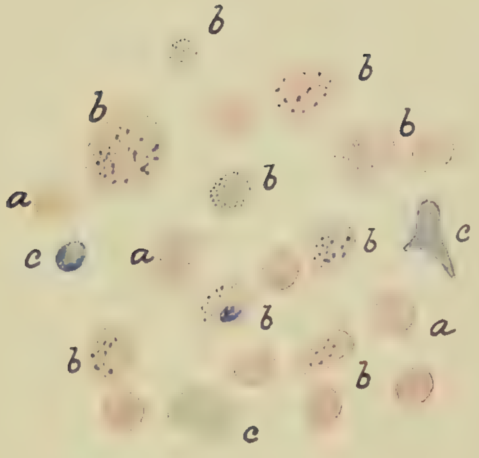

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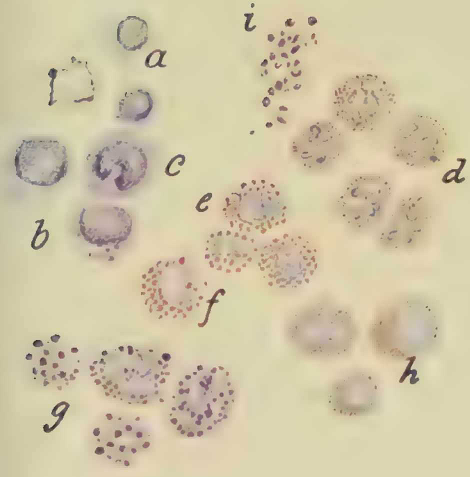

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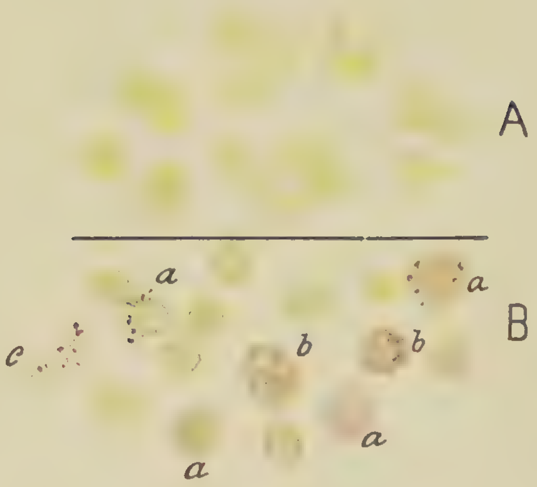

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Lymphocytes.—The small lymphocyte (Plate I, Fig. 3) is a cell about 7.5 μ in diameter, and consists of a spherical nucleus (rarely lobulated or divided) encircled by a narrow rim of protoplasm. Both the nucleus and the protoplasm are intensely basic, the latter usually the more so. The large lymphocyte (Plate I, Fig. 3), which is 10 μ or more in diameter, does not differ materially from the small form, save in size. Both types of lymphocytes are natives of lymphoid tissue, and are classed as nongranular cells, although exceptionally their protoplasm contains a few coarse metachromatic granulations. With these cells may be classed the so-called large mononuclear leukocyte, probably marrow-bred, and differing chiefly from the true lymphocyte in having a very slight basic affinity, especially of the protoplasm, which stains less deeply than the nucleus.

Transitional Forms.—This type of cell (Plate I, Fig. 3) resembles the large lymphocyte in size, but its nucleus is more basic, and indented, reniform, or crescentic in shape. The protoplasm is faintly basic and contains no actual granules. The clinical significance of the transitional cell is the same as that of the large lymphocyte.

Polynuclear Neutrophiles.—The polynuclear neutrophile (polymorphonuclear neutrophile; finely granular oxyphile) is a spherical or ovoid leukocyte 10 or 12 μ in diameter (Plate I, Fig. 3), with a single, twisted, lobulated nucleus of basic affinity (rarely with multiple nuclei), and a protoplasm densely crowded with fine neutrophile granules. These are the ε-granules of Ehrlich, which, though described as of "neutral" affinity, in reality have a faintly acid tendency.

Polynuclear Eosinophiles.—(Polymorphonuclear eosinophile; coarsely granular oxyphile.) This is a cell like the polynuclear neutrophile in size and general morphology, but differing in that the nucleus is less convoluted and less basic, and in that the protoplasm is studded with coarse eosinophile granules—hence the term "eosinophile," by which abbreviation this cell is commonly designated (Plate I, Fig. 3). The eosinophile or α-granules are intensely stained by an acid dye, such as eosin.

Polynuclear Basophiles.—But for the presence of delicate basic protoplasm granules and a distinctly less basic nucleus, this cell counterfeits in size and shape the polynuclear neutrophile (Plate I, Fig. 2). The granules, which stain with a basic dye, such as methylene-blue, are also known as δ-granules.

Myelocytes.—Of this pathologic variety of leukocyte (Plate I, Fig. 3) there are two types, the neutrophilic and the eosinophilic, the former being much the commoner. Each of these types of the myelocyte is from 10 to 20 μ in diameter, or even larger, and each has a relatively large nucleus which is usually of spherical contour, but sometimes is notched, constricted, or quite divided. The distinguishing feature of these cells is the granules embedded in their protoplasm, the neutrophilic myelocyte containing fine neutrophile granules, and the eosinophilic myelocyte, coarse eosinophile granules.

Mast Cells.—The mast cell (Plate I, Fig. 3) consists of a delicate spherical or ovoid nucleus surrounded by a mass of γ-granules which show an intensely metachromatic affinity, and vary in size from the finest stippling to a coarse cube. The nucleus, being almost structureless, shows scarcely any affinity for basic dyes, and the protoplasm is even more indefinable, so that the cell may appear simply as a collection of granules molded into a round mass varying in diameter from a minimum of 7 or 8 μ to a maximum of 20 μ.

Stimulation Forms (*Reizungsformen*).—These are cells of from 5 to 15 μ in diameter, with a single round basic nucleus of relatively small size and a non-granular protoplasm of a modified basic tendency. The exact significance of these stimulation forms is obscure, but they are known to invade the blood stream in association with the myelocytes.

Leukocytosis.—(Plate II, Fig. 1.) Leukocytosis is an increase above normal in the number of leukocytes in the peripheral blood, usually involving the polynuclear neutrophiles both absolutely and relatively, but exceptionally affecting all types of cells proportionately.* Thus, the criterion of a leukocytosis is not simply the *total number* of cells, but the *variety*, which accounts chiefly for the gain. To say that a blood-count shows 50,000 leukocytes per cubic millimeter may mean either leukocytosis or leukemia, but to add that 90 per cent. of this fivefold increase are polynuclear neutrophiles unquestionably means a true leukocytosis. Merely a relatively high percentage of polynuclear neutrophiles cannot be interpreted as a frank leukocytosis, as some writers profess to believe, upon wholly insufficient grounds.

Physiologic Leukocytosis.—Leukocytosis, usually of moderate degree and of brief duration, may depend upon numerous physiologic factors, the change here being attributable mainly to blood concentration and to peripheral stasis, rather than to stimulation of the hematopoietic organs. Increases due to such causes occur in the newly born, during digestion, during pregnancy and parturition, as a pre-agonal sign, and from various mechanical and thermal influences. The fact that causes such as these may account for a leukocytosis is always to be recalled in reading the blood report in a clinical light.

Pathologic Leukocytosis.—Leukocytosis is commonly associated with many pathologic states, chiefly those of infectious, inflammatory, and toxic natures, and in such instances the change reflects an overproduction of cells by the bone-marrow, in order thus to fortify the organism's defensive powers against disease. How this is accomplished has already been described in the chapter on Immunity (*q. v.*). The stage of actual leukocytosis (or *hyperleukocytosis*) is preceded by a brief period of diminution in the number of cells (or *hypoleukocytosis*), due to the initial shock of the irritant.

In disease the behavior of the leukocytes is an index to the intensity of the morbid irritant and to the individual's resisting powers. Regarded in this light and correlated with other clinical data, the leukocyte count often proves of the greatest practical value, but its interpretation as a pathognomonic sign, to the exclusion of the bedside symptoms, courts diagnostic disaster and sows the seed of hematologic skepticism. No qualified clinician cares to divorce the laboratory from the ward.

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* The term leukocytosis, as applied to a leukocyte increase regardless of the kind of cells involved, is perfectly justified by etymology, but usage and simplicity should restrict its use to a cellular increase affecting chiefly the polynuclear neutrophiles.

Clinically, it is convenient to consider pathologic leukocytoses etiologically, under these subheadings: (I) Inflammatory and infectious leukocytosis; (II) Post-hemorrhagic leukocytosis; (III) The leukocytosis of malignant disease; and (IV) Toxic leukocytosis. The leukocytoses experimentally provoked by the use of various chemicals, bacterial products, organic principles, and surface revulsives are of purely scientific interest.

I. Inflammatory and Infectious Leukocytosis.—Here are included the leukocytoses symptomatic of inflammatory and infectious conditions, of which abscess, sepsis, pneumonia, and scarlet fever are types. In such instances the behavior of the leukocytes is determined by these fundamental facts: (1) That infection or irritation of the human organism provokes a compensatory hyperactivity of the bone-marrow, whereby this tissue is stimulated to the overproduction and output of leukocytes, especially of the polynuclear neutrophile type, which, as disease-repelling elements, flood the blood-stream. (2) That the peripheral leukocyte count reflects the activity of this marrow reaction, which may be excessively stimulated, moderately excited, or entirely overwhelmed and stifled, according to the virulence of the irritant and the vital forces of the subject. In general terms, it is true that serous exudates are accompanied by less of a leukocyte reaction than purulent, and that acute disseminated inflammations excite higher counts than chronic circumscribed lesions. Fever *per se* is wholly without influence.

The following table serves to illustrate the leukocyte range in relation to the intensity of the irritant and the reaction offered by the individual.

DEGREE OF LEUKOCYTOSIS.	INTENSITY OF IRRITANT.	RESISTING POWERS.
Marked.	Marked.	Normal.
Slight.	Moderate.	Normal.
Slight.	Moderate.	Indifferent.
Absent.	Marked.	Feeble.
Absent.	Feeble.	Normal.

The most important factors of true inflammatory and infectious leukocytoses are tabulated herewith:

I. *General Infections.*

Asiatic cholera.
Bubonic plague.
Cerebrospinal fever.
Diphtheria.
Dysentery.
Filariasis.
Glanders.
Malignant jaundice.
Pneumonia.
Relapsing fever.
Rheumatic fever.
Scarlet fever.
Secondary syphilis.
Septicemia and pyemia.
Spotted (Montana) fever.
Tetanus.
Trichiniasis.
Typhus fever.
Vaccinia.
Varicella.
Variola.

II. *Local Lesions.*

Acute nephritis.
Actinomycosis.
Appendicitis.
Arthritis.
Bronchitis.
Burns.
Cholangitis.
Cholecystitis.
Dermatitis.

Endocarditis.
Enteritis.
Erysipelas.
Gangrene.
Gastritis.
Hanot's cirrhosis.
Hydatid disease.
Infected wounds.
Mastitis.
Meningitis.
Multiple neuritis.
Osteomyelitis.
Pancreatitis.
Pericarditis.
Peritonitis.
Purulent lesions.
Splenitis.

Post-operative leukocytosis, symptomatic of a reaction excited by the normal process of wound repair, follows surgical operations, and causes a moderate cell increase which develops immediately after the operation, attains a maximum usually within twenty-four hours, and disappears within from two to four days. A persistent leukocytosis beyond this period suggests infection, defective drainage, spreading inflammation, or hemorrhage. The influence of the anesthetic, the effect of hemorrhage, and the surgical cleanliness of the wound are side-lights always to be thrown upon the figures of a post-operative leukocyte count.

In contrast to the above-named factors of leukocytosis, there is also an important group of specific infections in which leukocytosis never occurs, except as the result of some complication. The diseases of which this is true are mentioned elsewhere. (See "Leukopenia," p. 129.)

II. Post-hemorrhagic Leukocytosis.—An acute, well-marked hemorrhage promptly excites a leukocytosis, usually distinguishable within a few hours after the blood loss and lasting for three or four days, in the average case. In fatal cases, however, the count may never exceed normal, or the increase may be so short-lived as to escape detection. Trauma, venesection, post-partum hemorrhage, and the rupture of an aneurism typify the exciting causes of this variety of leukocytosis. As a rule, little or no increase attends chronic hemorrhages—the hemoptysis of phthisis, the hematemesis of gastric cancer or ulcer, the oozing uterine fibroid, and bleeding piles rarely raise the count, probably because these moderate blood losses plus the individual's tolerance negative marrow reaction.

III. Leukocytosis of Malignant Disease.—The leukocytoses occurring in sarcoma and in carcinoma are due less to any specific toxicity than to coexisting infections and inflammations. In my experience about one-half of all cases of malignant disease show frank leukocytosis, and in all but about five per cent. the count is moderate. The change is likely to be most striking in large visceral growths with metastases, and least marked in small, superficial, local tumors. A further discussion of the blood findings in malignant neoplasms will be found in a subsequent section. (See p. 138.)

IV. Toxic Leukocytosis.—Here a non-bacterial toxic irritant causes the increase, the degree and persistence of which are explained by the theories applicable to infectious leukocytoses. The count is high in acute poisoning by ammonia, corrosive metallic salts, nitrites, alcohol, acetanilid, phosphorus, potassium chlorate, tansy, toluylendiamin, ptomains, carbon monoxid, and snake venom; in toxic forms of delirium and convulsions, *i. e.*, uremia, cholemia, and epilepsy; and in narcosis by ether and by chloroform.

Leukopenia.—A subnormal number of leukocytes in the peripheral blood is termed *leukopenia* or *hypoleukocytosis*. A physiologic type of

PLATE II.

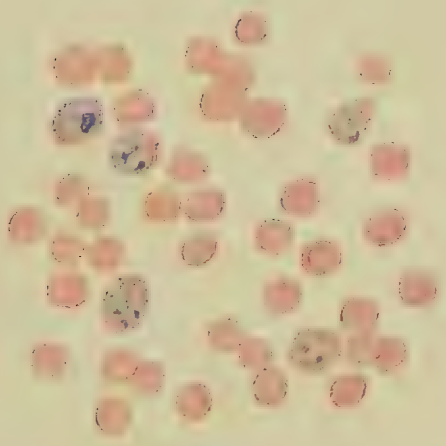

Fig. 1.—Leukocytosis.

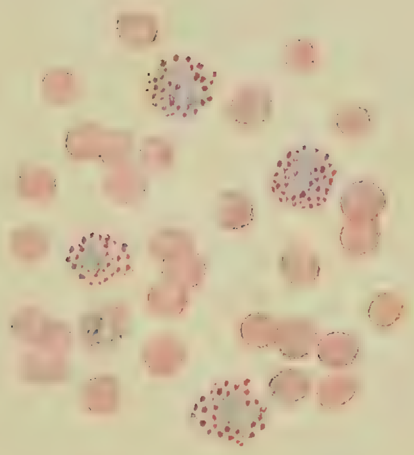

Fig. 2.—Eosinophilia.

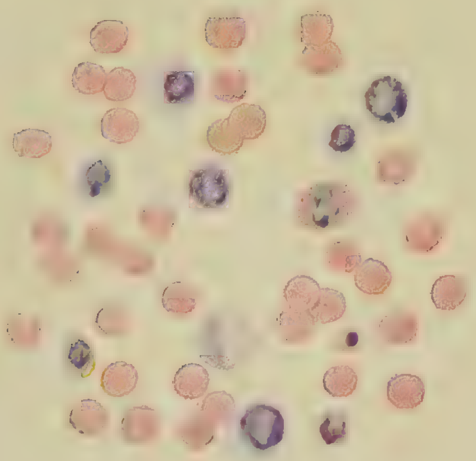

Fig. 3.—Lymphatic Leukemia.

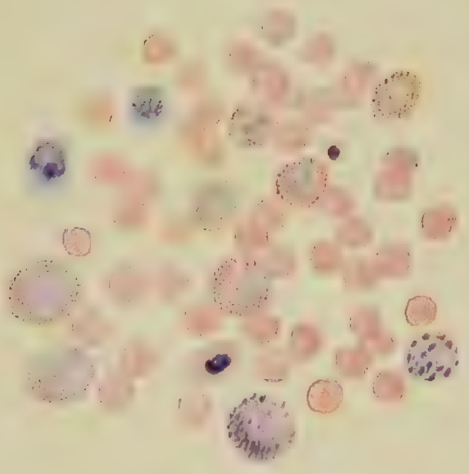

Fig. 4.—Myelogenous Leukemia.

(Wright's stain.)

leukopenia, depending upon a peripheral poverty of leukocytes due to vasomotor disturbances, is provoked by brief hot, and by prolonged cold, baths, by sensory nerve stimulation, and by lowered blood-pressure. Starvation and other conditions of malassimilation also are attended by a low leukocyte count.

The clinical significance of leukopenia in acute infections which ordinarily cause leukocytosis has already been described. In the following group of diseases, mainly infectious, leukopenia, or at least no leukocytosis, is the rule, save in the event of complications:

Chlorosis.
Enteric fever.
Hodgkin's disease.
Influenza.
Kala-azar.
Laennec's cirrhosis.
Leprosy.
Malarial fever.
Malta fever.
Measles.
Paratyphoid fever.
Peptic ulcer.
Pernicious anemia.
Rötheln.
Splenic anemia.
Sprue.
Trypanosomiasis.
Tuberculosis.

Experimentally, leukopenia may be induced by the administration of various anticoagulant substances and other agencies, chemical and organic, which destroy the cells. Rapid destruction of the leukocytes has been noted in animals exposed to the action of the Röntgen[41] rays, and the same thing occurs in leukemic persons thus treated. Neither radium rays nor ultraviolet light has any effect upon the leukocytes or the other elements of the blood.

Lymphocytosis.—(Plate II, Fig. 3.) Increase in the number of lymphocytes of the peripheral blood is termed lymphocytosis, a change which may be either relative, *i. e.*, due to a high percentage of lymphocytes without leukocytosis; or absolute, with both the lymphocytes and the total leukocyte count increased. Lymphocytosis is best accounted for by an activity of the lymphatic tissues, and by unequal distribution of the cells throughout the circulation.

Absolute lymphocytosis (lymphemia) is the blood picture of lymphatic leukemia, chloroma, pertussis, variola, and certain cases of infantile pneumonia. *Relative lymphocytosis* is a striking differential change in enteric, malarial, and Malta fevers; in trypanosomiasis, kala-azar, and other types of tropical splenomegaly; in tuberculosis, syphilis, rickets, scurvy, scrofula, and lymphosarcoma; and in some of the primary anemias. It also occurs after hemorrhage, after splenectomy, and as a pre-agonal sign. Relatively high lymphocyte figures are to be looked for in young children and in cachectic, debilitated conditions. It is generally true that diseases characterized by leukopenia also involve a relative lymphocyte gain, which being referable simply to diminution in the polynuclear neutrophiles, is really a fictitious change.

Eosinophilia.—(Plate II, Fig. 2.) This term means an increase in the number of eosinophiles in the circulating blood, and is due to the specific, selective action of a chemotactic irritant upon the eosinophilous marrow cells. With great constancy eosinophilia is found in helminthiasis, especially in trichiniasis, hydatid infection, filariasis, and intestinal worms; in various dermatoses; in diseases of the bones; in syphilis, bronchial asthma, chylous effusions, and myelogenous leukemia; and during the postfebrile period of acute pyrexias. A compensatory eosinophilia develops after splenectomy and in many lesions of the spleen. For a list of numerous other (reputed) factors of eosinophilia text-books on hematology should be consulted.

Subnormal eosinophile estimates are common in lymphatic leukemia, chlorosis, pernicious anemia, and tuberculosis; during the active pyrexia of most infections; after large hemorrhages; and as a pre-agonal blood change.

Myelemia.—The presence of myelocytes in the circulating blood, always a pathologic sign, is termed *myelemia* or *myelocytosis*. (Plate II, Fig. 4.) Myelemia, plus leukocytosis, is especially constant in myelogenous leukemia, in von Jaksch's multiple periostitis, and in malignant disease with bone metastases. Less commonly, the blood contains small numbers of myelocytes in the severer types of other anemias, both primary and secondary, and in those conditions associated with active leukocytosis. A trifling myelemia with marked anemia suggests a crippling of the marrow's hemogenetic functions, by fault of which imperfect, undeveloped polynuclear neutrophiles, of which myelocytes are the immediate ancestors, are to some extent produced; a striking myelemia with leukocytosis indicates that the marrow is so overstimulated in its endeavor to meet the call for polynuclear neutrophiles that these young myelocytic cells prematurely flood the general circulation. Both forms of neutrophiles, polynuclear and myelocytic, are believed to respond to identical chemotactic irritants. Similarly, the same irritants stimulate polynuclear eosinophiles and eosinophilic myelocytes, their parent cells.

Basophilia.—(Plate I, Fig. 2.) This word is applicable to an increase of the basophilic leukocytes in the blood-stream, a sign invariably to be regarded as pathologic and to be interpreted as the effect of a specific type of marrow stimulation. Enormous mast cell basophilia occurs in myelogenous leukemia, and a very moderate increase in many of the helminthiases, in Asiatic cholera, in the cachectic anemias, and in numerous dermatoses. I have found abnormally high mast cell figures in the primary anemias; in plumbism and Hanot's cirrhosis; and in actinomycosis, trichiniasis, filariasis, echinococciasis, and trypanosomiasis.

Iodophilia.—(Plate I, Fig. 4.) In numerous morbid states the dried blood film, when treated with iodin, shows many iodophile leukocytes or cells exhibiting an affinity for iodin. In such cells, generally polynuclear neutrophiles, the protoplasm is colored diffuse mahogany-brown or it contains discrete reddish-brown granules, while extracellular iodophile masses (possibly disintegrated leukocytes) also are observed. In an iodin-stained specimen of normal blood the leukocytes' protoplasm is tinged a pale lemon shade and their nuclei are colorless.

Iodophilia means simply toxemia, either bacterial or chemical, and probably denotes a form of leukocyte degeneration. It is a corollary of leukocytosis, and, like the latter, should be considered as symptomatic and not as pathognomonic. It is even more trustworthy than leukocytosis as a sign of infection, for grave toxemias which stifle leukocyte increases serve only to intensify iodophilia. Iodophile leukocytes occur in all purulent lesions attended with pus absorption, but they are absent in walled-off abscess. They are also present with great constancy in cryptogenic sepsis, pneumonia, and other infections; and in malignant disease, grave anemias, and severe cachexias. In enteric fever iodophilia may point to either intense infection or to hemorrhage, perforation, or other accident. In pure tuberculosis the reaction is negative. From a clinical standpoint, iodophilia suggests septic not tuberculous abscess, purulent not catarrhal appendicitis, septic not rheumatic nor tuberculous arthritis, malignant not benign tumor. Persistent iodophilia after the incision of an abscess indicates imperfect drainage; and after a pneumonic crisis, delayed resolution or some other post-critical complication.

Blood-plaques.—(Plate I, Fig. 3.) The blood-plaques or platelets are non-nucleated globular bodies, which tend to adhere in the plasma in racemose groups. They measure 1 to 4 μ in diameter, and are of amphophilic affinity, of quite obscure origin, and of wide normal numeric range—200,000 to 500,000 per cubic millimeter of blood, or even higher. Of their clinical significance little is known save that they are diminished in most of the acute fevers, in the hemorrhagic diatheses, in pernicious anemia, and in severe burns; and that they are commonly very numerous in many high-grade anemias (especially chlorosis and leukemia), as well as in most cases of pneumonia and tuberculosis. According to Cabot,[42] a decided plaque increase favors thrombosis.

Hemokonia.—These are colorless, refractive spheres of about 1 μ in diameter, and endowed with active whirling (non-ameboid) motility. Hemokonia are possibly nothing more than free granules extruded from the neutrophile and eosinophile leukocytes, and may have some bearing on immunity. These so-called particles of "blood dust" have no real clinical meaning, but it is known that they are especially abundant in typhus fever and in Addison's disease.

IV. SPECIAL SURGICAL HEMATOLOGY.

Abscess.—An abscess from which free absorption of toxic material occurs sooner or later causes a *secondary anemia*, the degree of which roughly measures the virulence of the poison. Chronicity of the lesion, low-grade resistance by the individual, and well-marked toxemia are the three factors which do the greatest damage to the hemoglobin and erythrocytes. Neither the size nor the site of the abscess determines the grade of the associated blood deterioration, although, other things being equal, the anemia is likely to be greater in deeply seated large abscesses than in those of superficial situation and of small size. Of 305 abscesses examined at the German Hospital, 62 (20.3 per cent.) had 50 per cent. or less of hemoglobin, while 20 (6.5 per cent.) showed an erythrocyte count of 3,000,000 or lower.

Leukocytosis also is determined by the grade of the toxemia. It may fail to develop, or if present, may suddenly decline as the result of an overwhelming poisoning of the patient. It is also absent when no reaction is excited, either because the lesion is benign or because it is effectually walled in by a pyogenic membrane. Extension of a pus focus is betrayed by an increase in, and adequate drainage by a disappearance of, the original leukocytosis. This table shows the range of the leukocytosis in relation to the site of the abscess in 451 cases:

SITE OF ABSCESS.	NUMBER OF CASES.	AVERAGE.	MAXIMUM.	MINIMUM.	PERCENTAGE OF CASES WITH LEUKOCYTOSIS.
Appendical	174	16,709	58,500	4,200	86.0
Pelvic	180	15,634	48,200	550	67.7
Renal	30	13,924	33,600	6,000	86.6
Superficial	32	13,600	17,850	4,800	78.1
Empyema	10	17,180	31,800	11,200	100.0
Cholecystic	9	18,891	21,200	9,500	88.8
Hepatic	8	14,922	23,400	9,300	75.0
Cerebral	8	11,428	18,500	6,800	75.0

In *general sepsis* the above changes also occur, but generally in a more conspicuous form. All cases of sepsis not showing leukocytosis are either very mild or exceedingly severe.

Iodophilia is also excited by the above factors of leukocytosis, but it is also seen in toxemia so marked as to stifle the cellular increase.

The association of leukocytosis, hyperinosis, and iodophilia points to pyogenic abscess rather than to tuberculosis exudate, gumma, hematoma, or benign neoplasm, and to purulent not serofibrinous inflammations. The blood is of no use in differentiating cerebral abscess, apoplexy, and acute meningitis, for each of these lesions may cause leukocytosis. An intense iodin reaction with high leukocytosis suggests that the patient, though decidedly toxic, is reacting adequately, while iodophilia with leukopenia indicates crippling of systemic resistance.

Sepsis, in contrast to enteric fever, malarial fever, and most cases of miliary tuberculosis, shows leukocytosis and a more rapidly developing anemia, but in distinguishing this quartette of infections blood cultures, the serum test, and search for the malarial parasite furnish the most important hematologic criteria. Iodophilia, it should be noted, may occur in all of these conditions.

Appendicitis.—Many cases of appendicitis are moderately *anemic*, and a few decidedly so, the change being attributable to the effect of sepsis and to the patient's debility, aside from the appendical lesion. In 139 German Hospital cases the hemoglobin averaged 69.5 per cent., and the erythrocytes, 4,295,955 per cubic millimeter.

The *leukocytes* are not increased in number in most cases of catarrhal appendicitis, yet occasionally a moderate rise (to 16,000 or 18,000) is met with, doubtless as the result of a circumscribed periappendical peritonitis. In appendicitis with abscess, gangrene, or general peritonitis well-marked leukocytosis is the rule, except in fulminant cases and in those in which an appendical abscess is so thoroughly walled in by a pyogenic membrane that no toxins enter the circulation. These figures, relating to 250 cases in the German Hospital, illustrate the leukocyte range in these two general types of the disease:

	Non-purulent* (76 Cases).	Purulent† (174 Cases).
Average	9,247	16,709
Maximum	17,100	58,500
Minimum	1,600	4,200
Counts above 20,000	None.	40
Counts of 10,000, to 20,000	31	110
Counts below 10,000	45	24

From the above data it appears that *average* counts in purulent cases about equal the *maximum* counts in the non-purulent; that simple catarrhal appendicitis does not raise the count higher than 20,000, but, roughly speaking, one-fourth of all purulent cases do so; that normal or subnormal figures are not incompatible with suppuration, gangrene, and their sequels; and, finally, that counts below 20,000 are no sure index to the character of the appendical lesion.

Analysis of almost 900 cases of appendicitis in the German Hospital justifies the following general deductions as to the diagnostic and prognostic significance of the leukocyte range in this disease.‡ In non-operative cases leukocytosis appearing during the early days of the attack suggests peritonitis, but the development of a leukocytosis after the first week is more likely to be symptomatic of appendical abscess. The sudden exaggeration of a leukocytosis already established betrays extension of the local lesion or of peritonitis, while the sudden decline of the count, with increasing acuteness of the other symptoms, signifies severe, perhaps fatal, toxemia. A stationary leukocytosis, with trifling fluctuations of the maximal figure, occurs in localized abscess, the count declining as the pus disappears or as it becomes walled in, and rising as suppuration extends and the process becomes periappendical. After operation, with adequate drainage, the leukocytes fall to normal within a few days, but with incomplete drainage they remain high, as they do also in cases with persistent peritonitis and other septic complications of the original appendical inflammation.

A normal leukocyte count or a moderate increase may be symptomatic of (*a*) simple catarrhal appendicitis, (*b*) circumscribed walled-off appendical abscess, or (*c*) fulminant appendicitis with severe toxemia. A well-defined leukocytosis may be met with (*a*) in appendical abscess imperfectly delimited by a permeable pyogenic membrane, (*b*) in appendical gangrene, and (*c*) in peri-appendical and general peritonitis. Upon the interpretation of the leukocyte count under these diverse circumstances the question of iodophilia sometimes has an important bearing. In the absence of iodophilia it is quite safe to conclude that no serious lesion of the appendix is present, although a positive reaction does not invariably imply the existence of an active inflammation.

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* Including catarrhal and interstitial forms, obliterative appendicitis, and fecal and other concretions.

† Including cases with abscess, gangrene, perforative peritonitis, sepsis, etc.

‡ These deductions, it should be clearly understood, are invariably to be read in correlation with other phases of the clinical picture. The blood-count, like most other laboratory findings, is but the supplement of the bedside data, and to exploit it as a specific sign is to invite embarrassing clinical errors. It is quite as bad practice to diagnose appendicitis by leukocytosis alone, as it is to stamp every heart murmur as endocarditic, or all glycosurias as diabetic.

In differentiating appendicitis from other abdominal inflammations the blood gives little or no real help: in, for example, pyosalpinx, ovarian abscess, pyonephrosis, perinephritic abscess, hepatic abscess, gall-bladder empyema, cecal cancer, intestinal obstruction, and mesenteric thrombosis there may be identical degrees of leukocytosis and of iodophilia. The same statement applies with equal force, though not with equal frequency, to acute gastritis, renal and hepatic colics, and dysmenorrhea, which if provocative of active inflammatory changes, raise the number of leukocytes and render them sensitive to iodin. Lead colic, though it may excite leukocytosis, disfigures the erythrocytes with basophilic stippling, a change found only in appendicitis cases which are exceedingly anemic. Simple tapeworm, should it ape appendicitis, is generally betrayed by eosinophilia. Gastralgia, enteralgia, and ovaralgia cause neither quantitative nor qualitative changes in the leukocytes. Nephroptosis, ovarian cyst, and uncomplicated enteric fever may safely be excluded if the patient has a well-marked leukocyte increase.

Actinomycosis.—A low color-index anemia and well-defined leukocytosis occur in this disease, probably more as the result of secondary sepsis than of any specific infection by the ray fungus. Superficial lesions usually are productive of lower leukocyte counts than those deeply seated.

Anesthesia.—A trivial hemoglobin loss, moderate polycythemia due to blood concentration, and a slight increase in the number of leukocytes lasting for about twenty-four hours, follow *ether anesthesia*. According to Lerber,[45] the leukocyte count is above normal in 95 per cent. of cases, the gain amounting to about 4000 (Chadborne[46]) or 5000 (Da Costa; Kalteyer[47]) per cubic millimeter, and affecting all forms of cells proportionately.

In *chloroform narcosis* the blood changes are similar to those excited by ether, but they are more marked and persist longer. Solimei[48] found, after protracted chloroform narcosis, methemoglobinemia, a delay in the coagulation time, evidences of active hemolysis, and a diminution in the oxygen content of the blood.

The risk, real or reputed, of operating on a patient having a low percentage of hemoglobin has been discussed in a preceding section. (See p. 115.)

Anthrax.—The occasional detection of the anthrax bacillus in the peripheral blood is the only hematologic finding thus far reported. Nothing is known of the cellular changes, if any exist in this infection.

Burns.—Locke's studies[43] show that in persons severely burned marked polycythemia, high leukocytosis, and decided plaque increase develop within a few hours after the accident. The leukocytes show degenerative changes marked in parallelism to the gravity of the injury, and myelocytes occur in small numbers.

Chloroma.—A normoblastic type of *anemia,* of progressive character, is found in chloroma, and in most instances high absolute *lymphocytosis* and the presence of many myelocytes and eosinophiles. Exceptionally, the lymphocytosis is simply relative. From lymphatic leukemia chloroma must be differentiated by objective symptoms, since the blood changes may be identical. In such instances one should recall Dock's belief,[44] that chloroma is simply a malignant, highly neoplastic form of leukemia. Graves's disease may show moderate relative lymphocytosis, but never a high absolute increase of the lymphocytes.

Cholelithiasis.—The blood changes found in cholelithiasis are referable to the associated jaundice and to inflammatory and septic complications. Thus, in cases with jaundice *slow coagulation* is the rule; in 28 such instances I found an average coagulation time of ten minutes and forty seconds, while in twelve cases without jaundice the average was five minutes and twenty-four seconds. It has not been proved that the delayed clotting of jaundice due to gall-stones predisposes to hemorrhage, though this is undoubtedly true of the toxic jaundice due to malignant disease of the biliary passages.

The *anemia* is seldom marked, except in septic cases, in which extremely low hemoglobin and erythrocyte figures are found. Of 136 hospital cases of gall-stone, the hemoglobin was 50 per cent. or less in 13 (9.5 per cent.), and the erythrocytes 3,000,000 per cubic millimeter or lower in 17 (12.5 per cent.).

Leukocytosis and *iodophilia* are rather common in gall-stone, owing to the frequency of complications. The former occurred in 35 (25.7 per cent.) of the above series, always as the result of marked jaundice, or of some complication, such as empyema of the gall-bladder, purulent and septic cholangitis, or peritonitis. The incidence, degree, and duration of the leukocyte changes are obviously determined by such factors as these.

A high leukocyte count suggests some complication of cholelithiasis; but a low count does not necessarily imply simple gall-stone, though when qualified by a negative iodin reaction such an inference is most strong. The blood is no criterion in distinguishing hepatic and renal colics.

Enteric Fever.—*Bacillemia,* a positive *serum reaction,* well defined secondary *anemia,* and *leukopenia* with lymphocytosis are the helpful hematologic findings in this infection. *Iodophilia* also develops in about one-half of all uncomplicated cases, and in practically all of those secondarily septic. To the surgeon this blood picture is of interest, first because of its bearing upon the initial diagnosis of typhoid; and, second, on account of its relation to the various surgical complications of the disease. The clinical pertinence of changes in the coagulation time of the blood in typhoid has already been noted. (See p. 112.)

Sepsis and trichiniasis are the two surgical diseases which perhaps most closely counterfeit enteric fever in their general symptomatology. But in septicemia blood cultures usually yield pyogenic cocci, the Widal test is negative, leukocytosis is the rule, and the anemia is more acute in development and in degree. Trichiniasis is characterized by decided leukocytosis with eosinophilia, and by negative results from blood cultures and the serum test.

Of the intercurrent surgical complications which alter the blood picture of typhoid, hemorrhage, perforation, and secondary purulent and septic lesions are the most important. *Intestinal hemorrhage,* if severe, causes a prompt and appreciable exaggeration of the anemia already present, though in the great majority of instances the blood loss is not sufficiently great so to act. Leukocytosis develops in most cases within a few hours after the hemorrhage, and persists for a variable period, depending upon the extent of the bleeding and upon the patient's reaction. (See "Posthemorrhagic Leukocytosis," p. 128.) *Intestinal perforation* excites leukocytosis, provided that the shock is not too great—a proviso which unfortunately robs this sign of diagnostic value in fully one-half of all cases. Aside from this, the cellular increase may be so transient as to escape detection, unless an almost hourly count is made. In Manges recent report[49] of sixteen cases of perforation with leukocyte counts, these cells rose in seven, of which three recovered; fell in three, all of which died; and remained practically unchanged in six, of which one recovered. These figures corroborate Thayer's earlier statement[50] that the prospect of relief from surgical interference is best in cases with leukocytosis, the absence or disappearance of which indicates malignancy of the infection and prostration of the patient. The rapid decline of a frank post-perforative leukocytosis, *pari passu* with an aggravation of the other symptoms, means a fulminant peritonitis plus a low ebb of the patient's vitality.

Of the secondary *purulent* and *septic lesions* exciting leukocytosis and intensifying iodophilia, the most important surgically are empyemata of the gall-bladder and of the thorax, suppurative arthritides, periostitis, osteomyelitis, purulent otitis media, mastoiditis, parotid bubo, septic thrombosis, and bed-sores. Complicating pneumonia and meningitis also affect the blood similarly.

Fractures.—In simple fractures a slight, transient *leukocytosis* sometimes develops, though more cases are encountered without this sign than with it; complicated fractures may give higher counts, which, however, do not exceed 15,000 or 16,000 per cubic millimeter, according to the experience of Blake, Hubbard, and Cabot.[51] *Lipemia* has been detected in fractures of the long bones lacerating the fatty marrow, with and without associated signs of fat embolism.

Hemorrhage.—*Oligemia* is the immediate consequence of an acute hemorrhage, and during this stage the blood, though of lessened volume, shows no corpuscular changes. *Hydremia* follows, as reaction sets in, and now the hemoglobin and erythrocyte values begin to fall, as the reëstablishment of the blood volume progresses by transfer of fluid from the tissues into the vessels. Even after this has occurred a further hemoglobin and erythrocyte loss takes place, so that several days elapse before the stable minimum of the anemia is attained. That an extraordinary degree of anemia after hemorrhage may be compatible with life is shown by the complete recovery of Hayem's patient[52] with but 11 per cent. of erythrocytes, and of Béhier's[53] with 19 per cent. of cells, following uterine hemorrhages. Leukocytosis (*q. v.*), striking increase in the number of plaques, and acceleration of the clotting time are other post-hemorrhagic findings.

Regeneration of the blood, according to Bierfreund,[54] is complete within four weeks after the hemorrhage if the hemoglobin loss does not exceed 25 per cent., and within three weeks if it is not greater than 20 per cent. The duration of this period of blood repair depends upon many factors, of which the extent of the blood loss, the native reactive powers of the individual, and the question of associated disease are the most important. Transfusion hastens regeneration, and may even stimulate it so actively that the blood values mount higher than the maximum normal point (Hall and Eubank;[55] Otto[56]). As regeneration proceeds, the deficiency of erythrocytes is made up much more rapidly than the hemoglobin loss, so that a low color-index persists for some time after the hemorrhage. During the period of regeneration the cyclical appearance of large numbers of normoblasts, known as "blood crises," is thought to be a sign of active and normal hemogenesis, for these phenomena frequently are followed by substantial gains in the hemoglobin and cellular figures. Owing to the abnormally active type of hemogenesis incident to hemorrhage, many of the cells thrown into the blood-stream are faultily formed and highly vulnerable—hence the occurrence of deformed, hydropic, and atypically staining cells, especially during the early stages of the regeneration period.

In hemorrhage versus shock, the detection of a lowered blood density and a subnormal hemoglobin percentage suggests the former, while in the latter the specific gravity is increased and the hemoglobin value unaltered. These findings apply, of course, only to pure, uncomplicated types of these accidents, and are therefore seldom applicable in a clinical sense. Mummery,[57] Sherrington and Copeman,[58] and Malcolm[59] should be consulted for accounts of the blood changes secondary to shock.

Intestinal Obstruction.—Leukocytosis promptly develops after intestinal obstruction, being symptomatic either of autointoxication or of gangrene and peritonitis. Bloodgood[60] believes that a count of 20,000 or 30,000 three or four days after the beginning of symptoms is a favorable sign for operative interference, but that if the leukocytes are below 10,000 at this time, it is probable that extensive gangrene-peritonitis has occurred. As a rule, a high count during the first twenty-four hours of the obstruction, followed by an abrupt decline in the leukocytosis within the next day or two, is highly suggestive of peritonitis and gangrene, in the absence of which complications the count remains at its maximum for four or five days and then gradually falls to normal.

Jaundice.—The *slow clotting* of the blood in conditions of icterus has been sufficiently referred to elsewhere. (See p. 112.) In the Jefferson Hospital there are records of four fatal cases of post-operative hemorrhage in jaundice due to cancer of the bile-ducts. Simple catarrhal jaundice has little or no effect on the blood, the *anemia* being ordinarily trifling, except in strikingly toxic cases, and the *leukocytes* normal in number in fully four-fifths of all cases. In forty cases I found seven (17.5 per cent.) with a hemoglobin percentage of 50 or less; nine (22.5 per cent.) with an erythrocyte count of 3,000,000 per cubic millimeter or lower; and eight (20 per cent.) with a leukocyte count in excess of 10,000 per cubic millimeter. Leukocytosis with jaundice suggests cholemia, pus, or cancer—not a simple inflammation of the biliary passages.

Malignant Disease.—A stubbornly persistent *anemia* is a hallmark of carcinosis, especially in its later stages, and in growths interfering with assimilation and nutrition, as in cancer of the esophagus and of the stomach. The hemolytic action of cancer toxins, discovered by Kullman,[72] explains the cachectic anemia of carcinoma not implicating organs directly concerned in body nutrition. Of one hundred and fifty-five cases of various types of carcinoma which I have analyzed, forty-five (29.0 per cent.) showed 50 per cent. or less of hemoglobin, and forty-three (27.7 per cent.) an erythrocyte count of 3,000,000 or lower. The average blood deterioration is more striking in carcinoma than in sarcoma, and in the individual case of the former far more conspicuous anemia frequently is encountered. Of forty-two sarcomata, but eight (19.2 per cent.) had a hemoglobin percentage of 50 or less, and only five (11.9 per cent.) an erythrocyte count of 3,000,000 or lower.

The *leukocytosis* of malignant disease is by no means constant, for it depends not so much upon the action of specific irritants as it does upon such factors as inflammation, sepsis, and hemorrhage. In my experience leukocytosis is almost twice as frequent in sarcoma as it is in carcinoma, 61.9 and 36.7 being the respective percentages of its incidence in the two types of tumors.

The following table shows the range of the leukocytes in one hundred and fifty-five cases of carcinoma:

SEAT OF TUMOR.	AVERAGE.	MAXIMUM.	MINIMUM.	NUMBER WITH LEUKOCYTOSIS.
Stomach, 75 cases.....	7,785	23,400	1,000	19 cases, or 25.3%
Uterus, 25 "	11,150	24,000	3,200	13 " " 52.0 "
Rectum, 16 "	8,921	16,000	6,000	4 " " 25.0 "
Breast, 18 "	10,163	31,500	5,200	6 " " 33.3 "
Liver, 10 "	17,549	40,800	8,000	8 " " 80.0 "
Intestine, 7 "	11,185	16,300	7,000	5 " " 71.4 "
Pancreas, 4 "	10,850	18,200	6,600	2 " " 50.0 "

From the above data it appears that the incidence and degree of leukocytosis are greatest in cancer of the liver, and least in cancer of the stomach and of the rectum. In gastric cancer *digestion leukocytosis* is absent in about 80 per cent. of all cases—a sign once believed to be of great diagnostic value in differentiating gastric cancer and ulcer, since in the latter digestion leukocytosis persists. The value of this sign is also negatived by the fact that it is occasionally absent in apparently healthy individuals and also in those suffering from various forms of gastritis.

In sarcoma leukocytosis occurred in twenty-six (61.9 per cent.) of forty-two cases examined, the average count being 12,386, the maximum 40,000, and the minimum 5000 per cubic millimeter. The general rule applies here (as it does in carcinoma) that small, inactive, superficial tumors show lower counts than large, active neoplasms implicating deep viscera.

Involvement of the bone-marrow by malignant disease is generally shown by well-defined *myelemia* and sometimes by *eosinophilia;* and of the lymphatic system, by *lymphocytosis.*

Other blood changes in malignant disease are the absence of *hyperinosis* and, in carcinoma, the presence of *hyperglycemia.* (See p. 120.) Loeper and Louste's claim,[61] that specific neoplastic cells invade the blood-stream in sarcoma, has not been corroborated; in no one of five cases have I been able to identify such cells.

In differentiating malignant and benign tumors the presence of persistent anemia and leukocytosis points to the former; abscess with sepsis may show identical findings, plus iodophilia and hyperinosis, which do not occur in malignant disease save in the event of septic complications. In malignant neoplasm of the liver versus amyloid disease, gumma, or Hanot's cirrhosis, high leukocytosis suggests the first; if hydatid disease exists, a high eosinophilia usually is found. The blood is an uncertain means of distinguishing cancer and ulcer of the stomach, although long-continued leukocytosis indicates cancer, since it occurs in gastric ulcer only as the result of digestion, of hemorrhage, and of perforation; high-grade anemia is also more common in cancer than in ulcer. The cachexias of malignant disease and of pernicious anemia are sometimes very similar, though the blood pictures differ, a high color-index, marked oligocythemia with megaloblasts predominating, and leukopenia with relative lymphocytosis being characteristic of the primary type of anemia.

Peritonitis.—Septic peritonitis constantly provokes *leukocytosis,* except in the mildest and in the severest cases; in the latter, however, *iodophilia* is most intense. Tuberculous peritonitis, except in early childhood, never causes a rise in the leukocyte count. The highest leukocytoses are found in purulent inflammations of the peritoneum, and in these high-grade secondary *anemia* also tends to appear. Of fifty-four cases of non-tuberculous peritonitis examined by me, forty-two (77.7 per cent.) showed frank leukocytosis, and forty (74.0 per cent.) well-marked anemia. The clinical pertinence of the leukocyte count in the peritonitides of enteric fever and of appendicitis is referred to under these diseases.

Protozoan and Helminthic Infections.—**Malarial Fever.**—Aside from the presence of specific hematozoa in the blood-stream, the malarial infections are characterized by anemia of variable intensity, by absence of leukocytosis, and by melanemia. The *malarial hematozoa* are animal parasites which invade the erythrocytes of the infected individual and there undergo an asexual phase of development ending in the destruction of their cellular hosts, in the liberation of newly developed parasites, and in the evolution of forms destined to be imbibed by the mosquito

(*Anopheles*), in which insect they pursue a sexual developmental phase essential for their perpetuation. *Anemia,* due to the destruction of the parasitiferous cells and to the specific malarial poison, develops in all cases, and, according to the severity of the infection and its chronicity, attains a variable degree of intensity. The *leukocytes,* save for the transient rises attending the paroxysms, are not increased in number; they are, indeed, usually subnormal, and show a decided relative lymphocytosis. *Pigment,* both within the leukocytes and extracellular, is a distinctive finding in most cases of malaria.

The foregoing blood picture serves to distinguish malarial fever from sepsis, in which infection pyogenic coccemia, leukocytosis, and iodophilia give the sought-for clues. In differentiating malarial fever from enteric fever and from tuberculosis, each of which may induce blood changes identical with those of ague, information may be derived from blood cultures and from the serum test.

Filariasis.—The peripheral blood of individuals suffering from filariasis is infested with embryos of the *Filaria sanguinis hominis* bred by parental forms of the parasite lodged in some part of the deep lymphatic system. These embryos are graceful, delicate worms, consisting of a central granular body enveloped by a loose hyaline sheath, and possessing active motility, owing to which they incessantly move about in the plasma between the masses of blood-corpuscles. Like the malarial parasite, the filaria requires the mosquito (*Culex fatigans*) as an intermediate host, to insure its perpetuation. In the commonest variety of filariasis, due to the *Filaria nocturna,* the embryos cyclically invade the peripheral blood during the subject's resting hours, but retire to the deep circulation when he actively moves about.

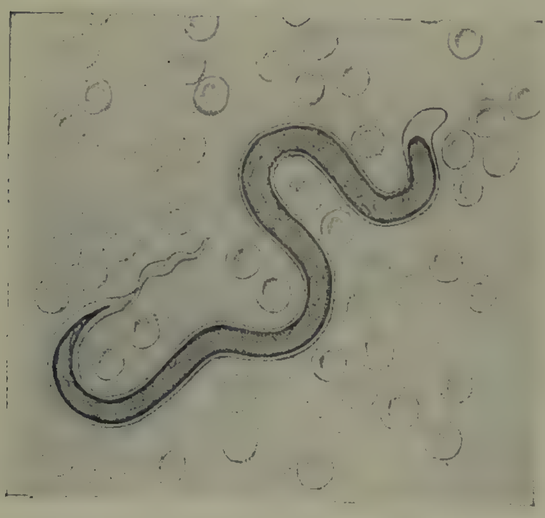

Fig. 29.—Filaria Sanguinis Hominis. Fresh blood film, showing granular degeneration of the parasite.

Anemia, when present, is traceable to some associated lesion, for the filariæ neither mechanically nor toxically affect the erythrocytes. The *leukocytes* show conspicuous changes—leukocytosis plus eosinophilia, each of which is marked in relation to the novelty of the infection, and tends to disappear in patients who have harbored the worms for some time.

The blood examination affords a means of differentiating filarial from idiopathic chyluria; lymph scrotum from hydrocele; filarial orchitis from other testicular inflammations; and hernia from filarial tumors of the groin. True elephantiasis Arabum, since it seldom causes a parasitemia, can rarely be distinguished from non-parasitic lymphedema by the blood, though a leukocytosis and an eosinophile increase are suggestive of the filarial form of the disease.

Trichiniasis.—*Leukocytosis* and *eosinophilia* constitute the hematologic formula of trichina infection, which of itself does not produce *anemia.* Eosinophilia, however, may be absent, as I have shown,[62] should the infection be so malignant as to suppress proliferation of the eosinophiles in the marrow, and it may disappear in cases of long standing, as in other forms of helminthiasis. Schleip's masterly monograph[63] should be consulted for the most comprehensive account of this subject.

The detection of an eosinophile leukocytosis serves to identify cases of trichiniasis otherwise symptomless, and to discriminate between those which resemble other infections, notably enteric fever. Absence of eosinophilia, on the other hand, is no criterion for ruling out trichiniasis.

Echinococciasis.—Like trichiniasis, hydatid disease causes an *eosinophile leukocytosis* without a specific anemia, no matter where the cysts may be situated. These changes promptly disappear after thorough evacuation of the cysts, and they gradually fade away in time, in cases not brought to the knife. Diagnostically, the above blood findings are of value in distinguishing hydatid tumors from pyogenic abscess and from solid tumors, provided that other factors of eosinophilia can be excluded.

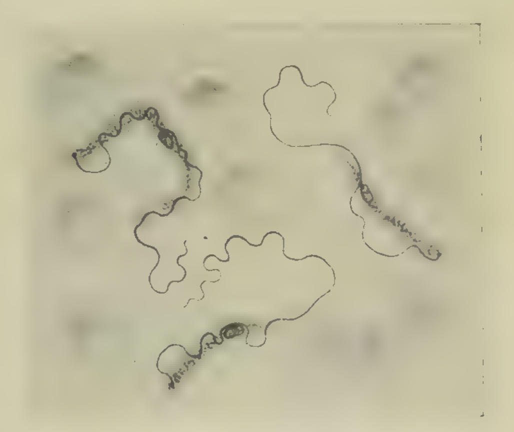

FIG. 30.—TRYPANOSOMA GAMBIENSE. (From a Leishman-stained specimen, furnished by the late Dr. J. Everett Dutton.)

Trypanosomiasis.—The demonstration of trypanosomata in the blood of human beings affected with tropical splenomegaly, sleeping sickness, and various cachexial fevers native to warm countries, has marked a brilliant advance in tropical medicine.* The parasite of man, termed *Trypanosoma gambiense,* is an actively motile protozoön, the body of which is provided with a delicate undulatory membrane and a whip-like flagellum.† The cultivation of trypanosomata *in vitro* from the Leishman-Donovan bodies of kala-azar, lately accomplished by Rogers[64] and by Chatterjee,[65] suggests the biologic entity of these two organisms.

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* The subject of human trypanosomiasis is inseparably associated with the name of J. Everett Dutton, who first discovered the organism in the blood of man, and adequately described its relation to disease. The recent untimely death of Dr. Dutton, while pursuing his investigations in the heart of the Congo region, has added another name to that noble roll of martyrs to science whose lives pay toll in the march of knowledge.

† For detailed descriptions of trypanosomiasis and its organism see the following important contributions: (1) *Nepveu:* "Compt. rend. Soc. biol.," Paris, 1898, v, 1172. (2) *Forde:* "Journ. Trop. Med.," 1902, v, 261. (3) *Dutton:* Brit. Med. Journ.," 1902, ii, 881. (4) *Dutton and Todd:* "Lancet," 1903, ii, 1727. (5) *Laveran:* "Compt. rend. Acad. d. sc.," Paris, 1904, cxxxviii, 841. (6) *Castellani:* "Brit. Med. Journ.," 1903, i, 1218, 1431. (7) *Koch:* "Brit. Med. Journ.," 1904, ii, 1445. (8) *Thomas:* "Brit. Med. Journ.," 1905, i, 1140. (9) *Rogers:* "Lancet," 1905, i, 1484. (10) *Bruce, Nebarro, Greig:* "Brit. Med. Journ.," 1903, ii, 1343. (11) *Dutton, Todd, Christy:* "Brit. Med. Journ.," 1904, i, 186; ii, 369. (12) "The Thompson Yates and Johnston Lab. Rep.," 1905, vi, 1. (13) *Greig, Gray:* "Reports of the Sleeping Sickness Commission of the Royal Society," London, 1905, v, 1.

Trypanosomiasis is accompanied by well-marked *anemia* and by relative *lymphocytosis* without leukocytosis—the same changes incident to malarial fever. The distinction, then, between these two types of protozoan infection rests upon the detection of the specific hematozoön.

Other Protozoan Diseases.—In amebiasis attended by hepatic abscess leukocytosis with more or less anemia develops, as in other suppurative states. In Schlayer's eleven cases[66] the leukocyte counts averaged 25,000, and in Futcher's[67] fifteen, 18,350 per cubic millimeter, but Osler[68] found that much lower figures were compatible with pus. In the question of malarial fever versus the intermittent pyrexia of hepatic amebic abscess, frank leukocytosis practically excludes paludism.

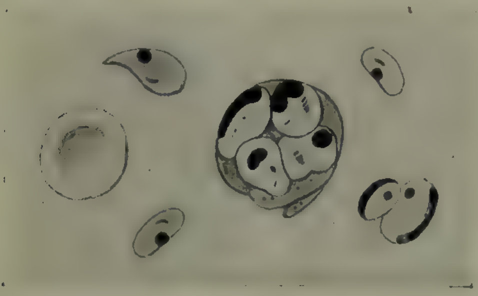

FIG. 31.—LEISHMAN-DONOVAN BODIES.

Other infections, such as kala-azar and the various intestinal helminthiases, have no special surgical pertinence. It is of interest, however, to note that all forms of intestinal worms are capable of provoking marked eosinophilia, and that some forms (notably the *Bothriocephalus latus* and the *Uncinaria duodenale*) set up anemia of a most striking type.

Syphilis.—The *Treponema pallidum* of Schaudinn and Hoffmann,[69] which possibly is the specific cause of syphilis, has been found not only in the local lesions of the disease, but also in the blood of the spleen and of the general circulation of luetic subjects. Siegel's *Cytorrhyctes luis*[70] is another supposed hematozoön which at present enjoys a certain vogue as the long-sought factor of syphilis. Of these two "organisms," Schaudinn's deserves the greater confidence. Siegel's cytorrhyctes strongly reminds one of those forms of dwarfed and fragmented erythrocytes found in anemic blood, especially in specimens which have remained exposed to the air for any length of time.

The *anemia* which exists in all cases of syphilis varies with the intensity and chronicity of the infection and with the effect of the specific treatment on the individual. In general terms it may be stated that in the primary stage of the adequately treated case the blood changes are like those of chlorosis, and that in the secondary stage moderate secondary anemia develops. In a neglected case of tertiary lues excessive blood impoverishment occasionally is found—the so-called "syphilitic pernicious anemia." Mercury, when administered for a fortnight or so, improves a syphilitic anemia, but when given continuously for a longer period it tends to act hemolytically, and therefore to aggravate the anemia. Marked hemoglobin deficiency in a mercurialized patient prognosticates intense symptoms as the disease matures. *Justus's reaction*,[71] a decided hemoglobin loss a few hours after a single inunction of mercury in a case of untreated syphilis, is in no wise pathognomonic. It sometimes fails to occur in early initial lesions, in undoubted secondary syphilis, and in latent cases; it may be positive in certain other non-syphilitic diseases.

Moderate *leukocytosis* sets in during the secondary stage, and in the anemia of tertiary syphilis a decided relative lymphocytosis is common, often associated with numerous myelocytes and perhaps with eosinophilia. In cases with high-grade anemia I have constantly detected *iodophilia.*

In distinguishing a severe syphilitic anemia from true pernicious anemia, the absence of a high color-index and of megaloblastic changes are sufficient to rule out the latter.

Tuberculosis.—The blood changes found in tuberculosis are referable to the influence of such factors as secondary pyogenic infection, malnutrition, and drains upon the body albumins, rather than to the disease itself, for a pure infection with Koch's tubercle bacillus causes practically no changes in the composition of the blood, save in the two exceptions noted below. The presence of *anemia* and *leukocytosis* in a tuberculous individual therefore suggests the existence of a secondary septic infection. A case of simple tuberculous adenitis shows a normal blood count, but so soon as the lesions soften and fistulate and become septic, the hemoglobin and erythrocytes begin to decline, the leukocytes to rise, and iodophilia to appear. The same is true when a secondary infection attacks a tuberculous hip, spine, kidney, or lung, none of which lesions in the absence of complications shows these blood changes. Unlike these forms of pure tubercle infection, tuberculosis of the meninges and, in the young child, of the peritoneum commonly excites well-defined leukocytosis during its acute phases.

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CHAPTER IV.

INFECTION AND IMMUNITY.

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INFECTION.

The Specific Microbic Causation of Infection.—At the present time the term infection is applied to "morbid conditions caused by the entrance and growth within the body of pathogenic microörganisms and to the act or process by which disease is thus produced." In this sense infection refers, not as it did at one time, to any particular mode of transmission of the morbific agent, but to its living nature and to its invasive mode of action.

In those infections whose etiology we understand best there is no doubt but that the essential disturbances in the infected subject are caused by microbic poisons, and in some cases these poisons alone may reproduce with great fidelity all the characteristics of the corresponding infection, except one, namely, transmissibility to other susceptible subjects. The reason for this is plain—the poison is incapable of multiplication. For this reason poisons whether produced by bacteria or other vegetable cells or by animal cells, are not included among the infectious agents proper, even though the symptoms and the lesions of intoxication sometimes cannot be distinguished from those of certain infections.

I have stated that pure intoxications are not transmissible. Under certain very exceptional circumstances human tetanus intoxication has resulted from the use of sterile antidiphtheric serum drawn from horses in the period of incubation following natural tetanus infection. In this case the serum injected contained enough tetano-toxin to cause tetanus. Spontaneous transmission of tetanus in this way is hardly conceivable.

The doctrine that infectious diseases are caused by microörganisms is centuries old, and was expressed with great clearness by Varro (116–27 B. C.). Undoubtedly the distinct individuality of many infectious diseases, *e. g.*, smallpox, early suggested the idea that these diseases are etiologic entities, but only in modern times has the existence of a specific cause been postulated for each infectious disease. This conception of specific etiology has dominated all recent investigation into the causation of infectious diseases. Pasteur, Koch, and their followers have furnished the positive evidence of the correctness of this conception for many infectious diseases, and we have every reason to believe that an infectious disease like measles or scarlet fever, which differs clinically and epidemiologically from other infectious diseases, must have its own peculiar living cause even though the search for that cause so far has been fruitless.

In order that it may be considered as absolutely demonstrated that a disease is caused by a specific microbe it is necessary to complete the chain of evidence formulated by Koch, namely: (1) The demonstration of the organism in all cases of the disease, and so distributed as thereby to throw light on the origin of the lesions. (2) The artificial cultivation of the organism in pure growth. (3) The reproduction of the disease by inoculation of the organism so isolated.

These three conditions, as is well known, have now been fulfilled in a number of human and animal infectious diseases. The most important human infectious diseases in this group are: tuberculosis, diphtheria, epidemic cerebrospinal meningitis, tetanus, anthrax, glanders, pneumonia, gonorrhea, bacillary dysentery, erysipelas, typhoid fever, Asiatic cholera, bubonic pest, and various inflammatory and pyogenic infections. In many of these diseases the third requirement—the experimental reproduction of the disease—has been fulfilled by means of animal experiments, but in certain cases, *e. g.*, gonorrhea, typhoid fever, Asiatic cholera, and dysentery, the final proof has been furnished by accidental or other inoculation of pure cultures into human beings, because animals, especially the smaller, are either insusceptible to the organism in question (gonococcus) or respond in a manner too divergent to be accepted as a satisfactory reproduction of the human disease (typhoid fever, cholera).

Recently Grünbaum has produced quite typical symptoms and lesions of typhoid fever in the chimpanzee by feeding of typhoid bacilli.

There is a large class of human infections, essentially inflammatory and pyogenic in nature, in which the requirements of Koch have been fully satisfied; these infections differ from the more sharply defined infectious diseases in that in many cases the same symptoms and the same anatomic lesions may be caused by more than one single bacterial species. Here belong acute endocarditis, pleuritis, peritonitis, meningitis, pericarditis, bronchopneumonia, bacteriemia, septicemia and pyemia, puerperal fever, acute arthritis, angina, other local inflammatory infections, and the infections of wounds. The different etiologic processes here included under collective names are slowly becoming more and more exactly defined as the results of careful observations by means of clinical, anatomic, and microbiologic methods.

In certain diseases the first two conditions only have been satisfactorily fulfilled, namely, influenza, actinomycosis, amœbic dysentery, oidiomycosis; and in others only the first requirement, the demonstration of the same organism in all cases—namely, leprosy, relapsing fever, piroplasmosis, trypanosomiasis, malaria, and probably syphilis.

Finally, there are a number of infectious diseases the causes of which have not been discovered—yellow fever, typhus fever, dengue, mumps, whooping-cough, smallpox, measles, scarlet fever, rabies.

As the mechanism of the pathogenic action of infectious microörganisms began to be studied other important means of proof of their etiologic relations was secured from the specific nature of certain reaction products that form in the infected organism—the antitoxins, the lysins, the agglutinins, and the precipitins—which may render most valuable assistance in the establishment of the causal significance of microbes.

In the last instance, however, the experimental production of the original disease by means of pure cultures under conditions that absolutely preclude the possibility of spontaneous infection must be regarded as the most conclusive proof of the specific etiologic rôle of a given organism and as essential in those cases in which the suspected organisms may belong to the so-called secondary invaders, which, as in smallpox, scarlet fever, whooping-cough, may cause no inconsiderable part of the symptoms and lesions and give rise to specific antibodies. Even though a definite organism is found to be constantly and exclusively present in the lesions of a disease, the possibility that it may be a secondary invader must not be overlooked.

The Various Forms of Infectious Microörganisms.—Infectious or pathogenic microörganisms may belong either to the animal or the vegetable kingdom. All animal pathogenic microörganisms are protozoa; the vegetable may be either fungi or bacteria. At the present time the bacteria are the most important infectious agents.

In addition to these well-established forms it has been discovered recently that certain highly infectious diseases, chiefly of animals, are caused by agents of as yet unknown nature that pass through bacteria-proof filters, and consequently are spoken of as filterable or ultra-microscopic virus. Foot-and-mouth disease, peripneumonia, rinderpest, sheep-pox, chicken-typhus, horse-sickness, epithelioma contagiosum in fowls, yellow fever, hydrophobia, possibly also vaccinia, and a form at least of hog cholera are thought to be caused by agents that probably are beyond the limit of microscopic vision, at least at some stage of their development. The only virus of this class that has been cultivated is that of peripneumonia, and in this case the elements are barely visible as particles under the highest powers of the microscope and by means of the so-called ultra-microscope.[1]

The most important human diseases caused by protozoa are malaria, amœbic dysentery, piroplasmosis, and trypanosomiasis (sleeping sickness). Human piroplasmosis has been described by Wilson aud Chowning,[2] but further work is necessary in order to establish the disease on an undisputed basis. Great interest has been aroused in trypanosomes, as well as in pathogenic protozoa in general, since Novy and McNeal [3] discovered a method by means of which they could be cultivated artificially. Amœbæ are also cultivable, but only in association with bacteria, which, however, may be of a definite species.

In comparison with the endless number and wide distribution of saprophytic bacteria there are in reality only few pathogenic bacterial species, and these, in common with other infectious agents, may be divided in three groups so far as their parasitic relations are concerned:

1. Obligate parasites, which develop only within a living host, *e. g.*, the bacillus of leprosy, the spirillum of relapsing fever, the protozoa of malaria, and the bacillus of tuberculosis. Although the latter may be cultivated artificially by certain special methods, it is not likely, however,

that it ever finds natural conditions suitable for growth outside the body.

The as yet unknown causes of the exanthematous diseases, of hydrophobia, of syphilis, are also regarded as obligate parasites; the agents of measles and scarlet fever appear to find suitable conditions for propagation within the human body only. In these cases, then, the parasitic adaptations are highly perfected and the perpetuation of the parasitic species largely dependent on their continued transmission from host to host.

2. Facultative saprophytes are ordinarily parasites, but are able to grow outside the body in dead organic matter. The majority of pathogenic bacteria belong in this group. No sharp distinction may be drawn between obligate parasites and facultative saprophytes.

3. Facultative parasites are ordinarily saprophytic, but capable of some degree of parasitic existence. The bacilli of tetanus, of anthrax, of emphysematous gangrene, and the amœba of dysentery, are facultative parasites, and in their case it appears to be a matter of indifference, so far as perpetuation of the species is concerned, whether they enter the living body or not.

It is generally regarded as most probable that bacteria and other microörganisms capable of adapting themselves to parasitic life have done so long ago, and that it is not likely that new diseases will arise from parasitic adaptation of forms at present saprophytic.

The most important pathogenic fungi from the surgical point of view belong to the ray fungi (actinomycetes, streptothrices, nocardia) and to the oidia (blastomycetes, oidiomycetes), the exact position of which in botanical classification probably has not been established.

The Sources and Ways of Infection.—As stated already, there are only few pathogenic species that are able to perpetuate themselves outside the animal body. Among the best known in this respect are the bacillus of tetanus, the bacillus of emphysematous gangrene, and the anthrax bacillus. In the case of the majority at least of the other pathogenic microbes the continuation of existence appears to be closely connected with or, as in some cases, wholly dependent upon the maintenance of definite parasitic relations.

Several pathogenic bacteria of particular interest in surgery are normally present upon the surfaces of the body without causing infections, however, except under very special conditions.

The common, most important source of the microbes of many infections is the sick man or animal, from which the microbe is transferred directly or indirectly to susceptible individuals.

Only the most important sources and ways of infection can be considered here.

Aërial Infection.—As infectious material reaches the exterior of the body in the secretions and discharges of the sick they may be deposited on the ground or floor, clothing, and articles of diverse character. So long as drying is incomplete, practically the only way by which they may spread disease is by means of direct contact, because air-currents cannot detach bacteria from moist surfaces, except possibly in the form of spray.

Until a few years ago aërial infection was regarded as due to dust particles carrying bacteria, but since 1897 the conveyance of bacteria in bubbles or droplets of sputum has received much emphasis, especially by Flügge and his followers.

True dust infection requires that the microbes in question withstand drying so that they are carried by the currents in our houses, hospitals, and operating rooms. Dry bacteria of this kind are the danger of dust infection as now understood. Strong currents and mechanical disturbances of accumulated material may set in motion larger particles, which, however, settle down rapidly, whereas the minute particles of completely dried material may remain suspended from three to four hours.

Neisser and others have shown that bacteria may be divided into three groups with reference to their infective power when dust-dried.

1. Those that are not viable in air-dried dust and that consequently cannot cause dust infection: cholera spirilla, pest bacilli, influenza bacilli, gonococci.

2. Those that withstand drying and hence may cause infections when conveyed in the currents of air in ordinary houses (1 to 4 mm. per second): pyogenic cocci, meningococcus, bacillus of tuberculosis, tetanus bacillus, and anthrax spores.

3. Those that can tolerate drying, but are disseminated only by currents stronger than those in our houses: diphtheria bacillus, typhoid bacilli.

It should be added that the causes of measles and scarlet fever may be transported in the air by cutaneous débris and other materials, but only for a distance of a few feet. In the case of smallpox, aërial convection is regarded as effective over a much larger territory.

Flügge and his co-workers have shown that in talking, coughing, or sneezing, germ-laden droplets or bubbles of sputum are expelled and may float about for some time. The distance to which the droplets may be carried depends on the expelling force, the air-currents, and the size of the droplets. Tuberculous patients rarely throw droplets farther than 1.5 meters, because of their size. After rinsing the mouth with prodigiosus suspensions Königer found that droplets might be carried so far as 12.4 meters. At present droplet infection is regarded as of more importance in spreading disease than dust infection. The specific agents of influenza, pneumonia, diphtheria, whooping-cough, measles, scarlet fever, smallpox, tuberculosis, and the bacteria of purulent infection are conveyed freely in this way. This mode of infection is of special importance to the surgeon.

Water-borne Infection.—Contamination of water with the discharges of infected individuals plays an important part in the spread of Asiatic cholera, typhoid fever, dysentery, and other diarrheal diseases, but in most waters, at least in temperate climates, the organisms probably can live for a very short time only under the conditions that obtain in nature. Prudden found that typhoid bacilli may survive in ice for 103 days. It should be remembered that there are various household uses of water, aside from drinking, through which infectious agents may be disseminated.

The Soil.—Pettenkoffer's theory that the soil played a peculiar and exclusive rôle in typhoid fever and cholera has been abandoned. It has been found by experiment that typhoid and cholera germs may retain their viability for some time after deposition in the superficial layers of the ground. Levy and Kayser found that the contents of typhoid contaminated privy vaults may be the means of disseminating living typhoid bacilli upon the soil even after the lapse of some months.

The natural habitat of the anthrax bacillus, the tetanus bacillus, and the gas bacillus is soil; the last two also occur in the feces of herbivorous animals and of man. Pathogenic staphylococci and streptococci have been found in the ground.

From the ground pathogenic germs may reach the body through dust, surface water, vegetables and fruits, flies and other insects, and by direct contact.

Food.—Food differs from some of the sources of infection just mentioned in that the pathogenic germs here may find excellent conditions for growth. These may be derived directly from animals supplying meat and milk, and the bacilli of tuberculosis (especially bovine), of anthrax, of glanders, as well as pathogenic streptococci and paratyphoid bacilli, may enter the body from this source.

Food, originally pure, may become contaminated; thus typhoid, dysentery, and diphtheria bacilli, cholera vibrios, and the cause of scarlet fever may be disseminated in contaminated milk.

Non-invasive but toxin-producing saprophytes may grow in milk, dairy products, meat, and fish, which on being consumed cause severe, often fatal cases of intoxication (food-poisoning, bromatotoxismus).

Infection through Animals.—Animals may be the means of causing human infections in three different ways.

1. Animals, especially domestic, may have diseases or harbor pathogenic germs that are directly or indirectly transferable to man, *e. g.*, those of anthrax, tuberculosis, glanders, pest. It is believed generally that the rat is the permanent source of bubonic pest.

2. Animals, especially flies and fleas, may act as mechanical carriers of germs that are deposited by chance here and there in such a way that contact or food infection of human beings occurs. Flies may play this part in spreading typhoid fever,[4] cholera, tuberculosis,[5] smallpox and possibly other diseases. Suctorial insects—*e.g.*, ticks, bed bugs, etc.—may carry infectious material from the sick to the well in biting.

3. Mosquitos act as intermediary hosts for pathogenic protozoa and organisms of unknown nature, which here complete certain developmental cycles, at the end of which they become infectious and cause infection when deposited in susceptible persons; this course is illustrated in malaria, yellow fever, filariasis, trypanosomiasis, and also by Texas fever in cattle.

Places of Entrance of Infectious Microbes.—Pathogenic microbes may enter the body by way of the skin and exposed mucous membranes, but only after overcoming certain obstacles to infection of these parts. When intact the skin is impenetrable to ordinary bacteria, but wounds, though ever so small, are a most important predisposing cause to cutaneous infection. Pyogenic cocci and other bacteria may settle in the glandular ducts and other parts and produce disease, but it is not believed that pathogenic microörganisms can invade the body through the healthy skin without first causing lesions at the point of entrance.

Pest bacilli cause general infection when applied to the shaven skin of the guinea-pig, but here, as well as in human pest, in which infection also occurs by way of the skin, it is impossible to exclude minute wounds.

Deep wounds with clotted blood and contused tissue, as well as crushing wounds, favor the lodgment of the tetanus bacillus and of the bacillus of emphysematous gangrene.

Healthy granulation tissue offers complete protection from ordinary infections.

The continuous shedding of the epidermis and the acid reaction of the perspiration are means of checking the growth of the bacteria that normally inhabit the skin.

The mucous membranes of the orifices of the body, and also in the mouth, the esophagus, and the vagina, are covered with laminated flat epithelium, and consequently probably as efficiently protected as the skin.

The conjunctiva, which is protected by the act of winking and by the tears, is frequently infected with various bacteria, and the experiments of Römer indicate that general infection may follow not from the conjunctiva directly but from the nasal mucosa. Small epithelial lesions, such as may be caused by dust particles, favor conjunctival infection.

The tortuous arrangement of the air-passages, especially in the nose, and the action of ciliated epithelium serve to protect the lungs from infection. The numerous folds and recesses, however, as well as the lymph nodes in the nasal mucosa, expose it to microbic invasion, and it is believed that meningococci and other organisms may pass from the nose to the meninges. From the nose infection may spread directly to the respiratory tract and by way of the Eustachian tube to the middle ear. Leprosy and glanders may develop primarily in the nose.

The mouth is guarded against infection by its dense lining and by the bactericidal and mechanical actions of the saliva and mucus. It is, however, the most common point of entrance of actinomycosis, the organisms of which are implanted into the gums about the teeth upon bits of straw and other vegetable particles. In reduced conditions certain anaërobes, normally present, may invade the tissues in association with streptococci and staphylococci and give rise to noma and, in the throat, to ulceromembranous angina.

The tonsils, though possessed, like lymph tissues in general, of properties hostile to many microbes, are important points of entrance of many infections. This may be explained, at least in part, by their exposed position, their irregularly indented surfaces, and their imperfect epithelial lining. Streptococci, pneumococci, and other organisms occur upon their surfaces normally. Acute articular rheumatism, infectious osteomyelitis, and other infections are often traceable to the tonsils by an initial angina. The tonsils are the common point of invasion of scarlet fever and of diphtheria, both of which are associated with an angina that usually is regarded as largely streptococcal in its nature. Undoubtedly the tonsils are the most important source of the general streptococcus bacteriemias that occur so commonly in smallpox and scarlet fever and also in diphtheria and other acute and chronic diseases. They are also important portals of entry for tubercle bacilli, especially early in life.

In many cases it is difficult to differentiate between pulmonary infections that take place from without and those by way of the blood and the lymph. It has been found, however, that tubercle bacilli, pneumococci, influenza bacilli, pest bacilli, etc., may be inhaled either in droplets or as dust particles, and thus cause pulmonary infections. Inhalation tuberculosis of the lungs is by far the most common form of primary tuberculosis. It is believed also that forced inspiration may carry pathogenic bacteria, *e. g.*, the pneumococci, from the mouth (and tonsils?) into the finer bronchi.

The gastric juice is a formidable obstacle to the passage of bacteria into the intestines, especially to organisms so susceptible to acids as the cholera vibrio. Koch and others show that feeding sheep with spore-free anthrax bacilli gives negative results, whereas feeding with spores results in anthrax. The gastric juice as well as the pancreatic juices destroy various toxins. Gastric disturbances, large masses of food, and fluid may serve to suspend or hinder the destructive or restraining influence of gastric juice upon pathogenic bacteria.

Several specific diseases have their portal of entry in the intestines, namely, Asiatic cholera, typhoid, dysentery, paratyphoid, and tuberculosis, as well as numerous epizoötics—anthrax, chicken-cholera, hemorrhagic septicemia. In typhoid fever, cholera, and dysentery the intestines appear to be the only point of localization, possibly typhoidal infection may occur by way of the tonsils. The reasons for this selective invasion are not understood. It is possible that paratyphoid bacilli are normal inhabitants of the intestinal tract that gain entrance into the tissue under special conditions only. Successful experimental infection by way of the intestines always requires large quantities of bacteria. It has been found that tubercle bacilli may pass through the gastro-intestinal mucous membrane without leaving any traces.

The genitals are the special seat of gonorrheal and syphilitic invasion; the gonococcus possesses the power to penetrate the urethral mucous membrane as well as other membranes lined with columnar or transitional epithelium. The vagina is well protected against infection by virtue of its squamous lining and the strongly bactericidal action of its secretion (Döderlein, Krönig and Menge). After birth the female genital tract offers good opportunities for infection because of traumatic lesions and the denudation of the uterus.

Certain pathogenic organisms are able to cause infection only when introduced in one way. Tetanus and hydrophobia originate from infection of wounds only, and the symptoms of these diseases become apparent after penetration of the specific toxin or agent into the central nervous system, for which it has special chemical affinities. The cholera vibrio and the dysentery bacilli localize in the intestinal epithelium only and the gonococcus on those parts of the genital tract that are clothed with cylindrical epithelium.

Similar affinities are shown in the further course of many infectious processes: streptococci frequently enter the blood- and lymph-stream, whereas cholera germs and influenza bacilli rarely leave the epithelium in which they are lodged. The causes for these various adaptations are as yet largely obscure; it seems that many organisms have become adapted to those parts of the body with which they come in contact in the course of natural infections. It is remarkable that those parts to which an organism is specifically adapted often contain the same microbe or closely related forms in an attenuated or harmless state.

The internal organs of healthy animals are regarded usually as sterile, but the recent investigations of Ford[6] and Wrzosek[7] indicate that in a large percentage of cases there may be an invasion principally of intestinal bacteria in health, but the relations of this latent microbism to actual infections and lesions are not yet clear.

Germinal infection—*i. e.*, infection of the embryo by agents conveyed either by the ovum or the sperm—takes place in the case of human diseases in syphilis only. Pébrine, a destructive protozoön disease of silk-worms, has been shown by Pasteur and others to be transmissible by germinal infection.

Intra-uterine or placental infection—*i. e.*, the passage of infectious microbes from mother to fetus—has been observed in the case of smallpox, measles, scarlet fever, syphilis, relapsing fever, pneumonia, anthrax, pyogenic infections, and tuberculosis. Various existing placental lesions, such as hemorrhages, necrosis, loss of chorionic covering, favor placental transmission. The circulation in the placental and uterine sinuses favors the arrest of bacteria that may be present in the maternal blood. Baumgarten's view that tuberculosis is frequently inherited, in the sense that there is an intra-uterine transmission of bacilli, which remain latent in the organs and tissues of the child until later in life, has not received general support. The number of cases of congenital tuberculosis is still small, and although Harbitz[8] has found latent tubercle bacilli in normal human lymph nodes, it is exceedingly hard to fix the possible duration of such latency, because of the many chances of postnatal invasion.

Elimination of Microbes.—Elimination of pathogenic microbes from the infected body may assume different forms that appear well adapted to continue the existence of the parasitic species and to spread infection. Consequently accurate knowledge of the ways and means of elimination is of the greatest value in preventing the dissemination of infectious diseases.

There are two main forms of microbic elimination, namely: (*a*) Immediate elimination from the seat of primary or secondary infection by way of pathologic products; (*b*) elimination from the blood through normal secretions and excretions or through the means of certain insects, as in the case of some protozoan parasites with highly specialized parasitic adaptations.

In the first case the diseased or infected part must stand in direct communication with the outside, as is the fact in all infections of cutaneous and nearly all mucous surfaces. The majority of the most important infections enjoy these favorable opportunities for self-propagation, as illustrated by local and general infectious processes with specific cutaneous lesions (suppurations, syphilis, tuberculosis, smallpox, measles, scarlet fever and other acute exanthematous diseases); by infectious conjunctivitis; by infections that localize upon the lining of the nose, *e. g.*, leprosy, glanders, influenza, pyogenic processes, and upon the tonsils and pharyngeal membrane, *e. g.*, diphtheria, scarlet fever, smallpox, measles, streptococcal and other forms of angina; by laryngeal, bronchial, and pulmonary infections (tuberculosis, pneumonia, influenza, whooping-cough); by intestinal infections (typhoid fever, dysentery, cholera, tuberculosis); and by infectious processes of the genito-urinary passages, especially gonorrhea and syphilis. During the process of elimination there is danger of auto-infection, illustrated especially well in tuberculosis.

The prevention of infectious diseases by disinfection of materials in which pathogenic microbes are eliminated offers many problems of great practical importance and difficulty, especially so far as sputum and nasal secretions are concerned.

In the second form of elimination the microbes are carried by the circulation to various glandular organs and mucous membranes. Bacteria regularly enter the circulating blood in typhoid fever, pest, pneumonia, and general septic infections, and while great numbers of such bacteria no doubt are destroyed by the bacteriolytic and phagocytic powers of the blood and blood-making organs, yet many are eliminated in the urine and otherwise. Thus, typhoid bacilli reach the urine frequently, as shown by the typhoid bacteriuria which thus is established in about 25 per cent. of all cases of typhoid fever, and which is a particularly dangerous means of spreading the disease, because it may persist for months and even years.

It is believed generally that some lesion of the kidney is necessary in order that bacteria may pass through it into the urine.

Typhoid and tubercle bacilli are eliminated in the bile, and experimentally bacteria may pass out of the circulation through the intestinal mucous membranes.

Tubercle bacilli occur not infrequently in the milk of tuberculous cows without the presence of demonstrable lesions in the udder.

The virus of hydrophobia passes into the salivary secretions, thus explaining well the infectiousness of the bites of rabid animals. In the same way is explained the danger of the bites of mosquitos harboring malarial organisms.

Under certain circumstances, the exact nature of which we do not understand, pathogenic organisms may persist in the body in a latent condition. In most cases it concerns survival of specific organisms after attacks of typhoid fever, pneumonia, malaria. In the two former diseases the surviving bacteria may manifest their presence by local inflammatory lesions, and in typhoid fever years may intervene between the primary disease and the late local manifestations. Recently staphylococci have been observed to persist in the blood for some time after recovery from staphylococcemia (Panichi), and Duval and Lewis[9] noted the occurrence of B. mucosus capsulatus in the blood of a patient who had recovered fully from a general infection with that organism. In immunized animals streptococci and pneumococci have been observed to remain in the blood for some time after injection without apparent symptoms. The bacteria here appear to pass into a kind of latent state in which they escape destruction at the same time as bacterial metabolism is largely suspended, or perhaps the tissues of the host are resistant to the toxic bacterial products. Theobald Smith[10] has emphasized the importance of these conditions in securing for the microörganism opportunities to escape into new hosts.

Mixed and Secondary Infections.—Mixed infections due to the simultaneous entrance of two or more virulent pathogenic species are most commonly observed in the parts of the body that communicate with the air and consequently always harbor numerous bacterial species. In pharyngeal diphtheria and scarlatinal angina streptococci enter the tonsils constantly and early; in diphtheria, for instance, Baumgarten regards the mixed infection as the rule. Bronchopneumonia from respiratory invasion is usually due to mixed infection of pneumococci, hemophilous (influenza) bacilli, streptococci and staphylococci, etc., in various combinations.

Wound infections are usually mixed infections.

Of late the mixed infections in which anaërobic bacteria are present have received special attention. The mouth and throat, the intestines, the genital canal in women, the preputial space, and the biliary duct normally contain a variety of anaërobic bacteria. Among the better known anaërobes of this class may be mentioned especially: (1) B. Welchii (B. aërogenes capsulatus), the common cause of abnormal gas production in the body, as seen in "foamy" organs, in gas cysts, pneumo-peritonitis, pneumaturia, physometra, and in emphysematous gangrene. The normal habitat of this bacillus is the intestinal tract and the soil. (2) The fusiform bacillus and spirilla of Vincent, found especially in the mouth and present in large numbers in a variety of necrotic and inflammatory lesions (Vincent's fusospirillar symbiosis), the most important being ulcero-membranous processes in the throat and mouth, and noma, but found also in hospital gangrene, fetid abscesses, and appendicitis.

Friedman[11] has shown that strict anaërobes are present constantly in the large intestine of man, and that probably some varieties become virulent under abnormal conditions.

French investigators, led by Veillon, have insisted for some years that strictly anaërobic organisms play an important though neglected rôle in many common inflammatory processes.

Under various conditions, such as trauma, placental retention, lithiasis, strangulation, previous aërobic infection, as well as general physiologic weakness, anaërobic bacteria may take part in the causation of inflammatory and gangrenous or putrid processes, usually accompanied with a fetid odor and concerning the intimate nature of which as yet in reality we are poorly informed. Strict anaërobes have been isolated from abscesses of the liver with and without suppurative pylephlebitis; abscesses of the abdominal wall; appendical abscesses especially; the exudate of general peritonitis; gangrenous appendicitis; putrid infections of the female genital tract; gangrenous processes in the lungs; putrid pleuritis; suppuration in the middle ear and mastoid cells; gangrenous tonsillitis and noma.

When aërobic cultures are made from the pus or exudate in these lesions, pyogenic cocci and colon bacilli are obtained as the usual rule, though sometimes only in very insignificant numbers. Anaërobic cultures, however, may show abundant growths, especially when gangrenous and fetid processes are present. In fact, Rist[12] claims that purely aërobic suppurations, as a rule, are free from fetor, and that suppurations in which anaërobic organisms are present as a rule are fetid.

Commonly a variety of anaërobic bacteria occurs in the processes just mentioned, and that all are not necessarily saprophytic but in themselves pathogenic is indicated, first, by the experimental production of gangrenous processes by injection of pure and mixed anaërobic cultures (Rist), and, secondly, by the occurrence of anaërobes in spontaneous processes, either in preponderating numbers or to the complete exclusion of anaërobes. Harris obtained a strictly anaërobic bacillus (Bacillus mortiferus) from hepatic abscess in man. This bacillus has peculiar and well-marked pathogenic action on animals.

Concerning the nature of the toxic substances probably produced by these anaërobes we as yet have no information, and the subject merits further investigation.

The knowledge that anaërobic bacteria may be concerned in suppurations is of practical value in that it carries with it the indication to use oxidizing agents as well as free exposure to the air in the treatment.

Established primary infections frequently appear to prepare the way for secondary mixed infections. All diseases that lead to destructive lesions of the skin and mucous membranes (variola, typhoid fever, tuberculosis, etc.) favor directly invasion with microbes normally present in the body (streptococci, pneumococci, staphylococci, colon bacilli), and there is good reason also to believe that infectious diseases generally lead to diminution in the normal powers of the body to resist infection.

Smallpox, scarlet fever, measles, tuberculosis, diphtheria, are associated so commonly with other infections, especially streptococcal, that there can be no doubt of the existence in these diseases of specially favorable conditions for streptococcal invasion. The rôle of general weakness in the establishment of anaërobic infections has been mentioned. Examples are not wanting of mixed bacterial infections in protozoan diseases and vice versa.

Associated infections have been grouped as follows on the basis of the distribution and fate of the organisms concerned: (1) The associated infections may remain localized (mixed local infections). (2) Dissemination of primary and secondary invaders, *e. g.*, general secondary streptococcus infections in miliary tuberculosis. (3) The primary invader remains localized and may disappear, while secondary invaders extend, as seen in the secondary streptococcemia of many infections, especially in smallpox and scarlet fever. Not infrequently secondary lesions, sometimes metastatic in character, may develop after the primary infection has subsided. (4) The largest group is that in which the chief organism becomes disseminated, whereas the mixed, secondary invaders remain localized. It is illustrated by the local suppurative infections that occur so commonly in all infectious diseases.

In human pathology we have no indications that one infection is really antagonistic to any other infection. There is reason to believe that bacterial associations in many cases tend to increase the virulence of one or other of the associated species. In infectious diseases generally the advent of secondary infection increases the danger to the patient.

The Mechanisms of Pathogenic Microbic Action.—The direct effects of pathogenic microbes upon the cells and tissues of the infected body are essentially chemical in their nature. The doctrine of microbic intoxication received its first substantial support by the discovery in 1888 by Roux and Yersin of the toxin of the bacillus of diphtheria, and by Kitasato soon after of the toxin of the bacillus of tetanus, both being substances that in susceptible animals cause the symptoms and lesions characteristic of the respective infections.

Since then it has become established that toxins, strictly speaking, are soluble poisonous products of bacterial, vegetable, and animal origin; their exact chemical nature is not yet understood, but they resemble much the organic ferments in being very sensitive to heat and other external influences; the toxic effects of toxins become apparent only after a variable period of latency; like many organic ferments, toxins also under suitable conditions and in susceptible animals give rise to the formation of specific antibodies, antitoxins, that neutralize the respective toxins *in vivo* as well as *in vitro*.

These characteristics serve to distinguish true toxins from certain other poisonous substances concerned in infections.

In addition to diphtheria toxin and tetanotoxin which are the most important bacteriotoxins, true toxins, many with a rather limited range of activity, have been demonstrated in cultures of B. botulinus, B. pyocyaneus, B. anthracis symptomatici, Staphylococcus aureus and albus, streptococcus, pneumococcus, and other bacteria. Some of these toxins cause laking of red blood-corpuscles (bacterial hemolysins).

Many bacteria produce more than one toxin; thus, the tetanus bacillus gives rise to tetanospasmin and tetanolysin; staphylococci and streptococci produce both hemolytic and leukocidal toxins.

Of the vegetable toxins ricin, abrin, robin, and krotin have been of great value for experimental investigations, especially by Ehrlich, of fundamental problems of toxic and antitoxic action.

Powerful toxins occur also in the venoms and other secretions of poisonous animals.

It is now generally accepted, in accord with Ehrlich's lateral-chain theory, that the toxic action of bacterial and other toxins is the result of a chemical union of the toxin molecules with certain cells. It has been shown, for instance, that tetanus toxin is quickly taken up by the nervous tissues, both inside and outside the body (Wassermann and Takaki), and the hemolytic toxins are absorbed by the red corpuscles, which then undergo laking. This union between toxin and cell is assumed in Ehrlich's theory to take place by means of free side chains or receptors in the cells in which are fitted, so to speak, free groups in the toxin molecules, the cytophile or haptophore groups. After the union the toxic action is accomplished by toxophore groups.

Many pathogenic bacteria do not produce enough soluble toxins in the usual cultural fluids to account for the symptoms and changes in the infected body. In the case of some, distinct toxic effects independent of injection are demonstrable only by the injection of dead germs or crude derivatives thereof. Here belong streptococci, pneumococci, the cholera vibrio, and the bacilli of tuberculosis, typhoid fever, dysentery, and plague.

It is believed by many that in these organisms the pathogenic substances are firmly attached to the bacterial cells and set free only as the bacteria undergo destruction in the host. These substances are called endotoxins, but differ from true toxins in that so far it is doubtful whether antiendotoxins have been obtained.

Welch[13] has advanced the theory that in the host the bacteria of this group are stimulated to produce toxic substances of the nature of amboceptors.

Vaughan[14] suggests that in the infected body groups are split off from the bodies of the bacteria, some of which he has succeeded in splitting up into distinct molecular groups. Thus the colon bacillus yields toxic, hemolytic, carbohydrate, and nuclein groups. Whether the toxic bodies isolated in this way are the active pathogenic substances of the bacteria in question is as yet unsettled.

Bacterioproteins in general when injected give rise to local changes of inflammatory nature, to fever, and also, as a rule, to a general leukocytosis, but the differences in these changes show that different bacterioproteins possess certain specific properties.

In the so-called intestinal putrefactions that may occur in infections there may develop substances that when absorbed cause more or less severe intoxication. Harmful products may result also from the splitting up by bacteria of dead cells, exudative and other materials in the body.

The metabolic disturbances of infections are caused in various ways. The anorexia and nervous disorders so common in infections diminish the intake of food; this may be associated with greatly impaired digestion and absorption, which, together with anemia and perhaps with respiratory disturbances, may lead to a condition of more or less well-marked inanition, with the characteristic alterations in the kind and the ratio of substances excreted in the urine and the expired air. Abnormal losses of substances often result from vomiting, diarrhea, hemorrhages, and to some extent from inflammatory exudations. Owing to disturbances in the osmotic relations there may be retention in the body of substances, some of them toxic, that ordinarily are eliminated. In the fever of infection the increased temperature alone naturally hastens dissociation of complex substances and the formation of the end-products of tissue metabolism. In causing the symptoms of infections the products of proteid decomposition no doubt play an important part that merits continued investigation, on account of the greater interest taken of late years in the specific reactions of infectious diseases than in the general or non-specific chemical changes.

Resistance and Virulence.—While microbes are the ultimate causes of infection there are many important etiologic factors relating to the individual exposed to infection. As pointed out, the animal body is possessed of various defensive mechanisms upon the condition of which depend to no small degree the individual resistance or susceptibility to many infections.

This individual susceptibility or predisposition comes more evidently into play in infections with organisms of medium or low virulence. Human beings are so susceptible to some diseases, *e. g.*, smallpox, measles, etc., that in these infections the factor of predisposition loses much of its importance.

Variations in susceptibility to infection may be due to variations in local factors, mechanical and chemical, that serve to protect against microbic invasion. Thus the skin is protective because when intact it is quite impenetrable to bacteria. The numerous bacteria vegetating on the surface are in large part carried away by the normal epithelial desquamation. The acid reaction of sweat is inimical to many bacteria. Coughing and sneezing, the outflow of fluids, the movements of the stomach and intestines, epithelial desquamation, the action of cilia, etc., are mechanical means of removing microbes from various mucous membranes. Other normal protective factors are illustrated by the toxin-destroying effects of the digestive juices, the bactericidal action of the gastric juice under the usual conditions in health, of vaginal mucus and of other glandular secretions, and by the antagonism to certain pathogenic forms on the part of the saprophytic organisms vegetating on mucous surfaces. This enumeration by itself suffices to indicate how comparatively slight disturbances of normal conditions may increase individual susceptibility to infection.

Wounds, necroses, hemorrhages, alterations in the secretions, trophic disturbances, may open the door for infectious organisms at the same time as they may lessen the physiologic resistance of the part involved. Favorable local conditions are especially significant when associated with an increased general susceptibility.

On reaching the interior of tissues microbes encounter normal defensive mechanisms, of which phagocytosis and bacteriolysis are understood best at present. These processes are discussed more fully in connection with immunity. As a consequence of inflammatory changes the protective agents concerned in these processes may be concentrated about the point of entrance or localization of infection. Microbes that are carried away in the lymph-stream become arrested in the corresponding lymph nodes, where they are subjected to attack by phagocytes and bactericidal substances.

Normal blood also contains antibodies, usually in small amounts, against various toxins, such as the hemolysins of streptococci and staphylococci and the leukocytic toxins (leukocidin) of the latter.

Now, upon the content of the blood in the substances necessary for phagocytosis (opsonins), in bacteriolysins, and in antitoxins, as well as upon the condition of the leukocytes, may depend in large measure the relative resistance of an individual to infection. The richer the blood of a given person in the means of destroying a given microbe and in neutralizing its toxic products, the greater must be his resistance to infection with that microbe. Absolute natural immunity to toxin is probably due to lack of suitable cellular constituents with which the toxin may unit. Thus Metchnikoff observed that in naturally immune animals tetanus toxin circulated free in the blood. Again, the toxin may be absorbed by cells of relatively little importance to the economy or upon which the toxin has little power.

Generalization as to the relative importance of bacteriolysis and phagocytosis is not worth much because the exact mechanism of resistance to the different pathogenic microbes is not yet understood well enough.

From test-tube and other experiments it may be inferred that typhoid bacilli, cholera spirilla, dysentery bacilli, and colon bacilli are destroyed especially by direct bacteriolytic action, whereas streptococci, staphylococci, pest bacilli, pneumococci, and anthrax bacilli in the dog, are not directly destroyed by the serum but by phagocytes after having been acted upon by the opsonins in the serum.

In view of the fact that the experiments of Hankin and Kanthack, Wassermann, and others show that bacteriolytic complement may be derived from leukocytes and because serum certainly is essential to phagocytosis, the antagonism between Metchnikoff's phagocytic and Buchner's humoral theories of general resistance has subsided, because neither phagocytosis nor bacteriolysis takes place without the conjoint action of both cells and fluids.

That leukocytes do play an important part in the defence against infection is clearly shown by the fact that in animals distinct protection against otherwise fatal doses of infectious material results from the injection of a variety of substances (serum, blood, urine, various proteid substances, yeasts, etc.) that have in common the power to stimulate leukocytosis.

General natural resistance may be diminished in different ways. Experimentally exposure to abnormal temperature, muscular exhaustion, diminished alkalinity of the blood, anemia, narcosis, alcoholic intoxication, hunger and thirst, phloridzin diabetes, preëxisting infections, the injection of lactic acid and other chemical substances, all reduce the resistance to various infections. We know that the complements and opsonins in the blood are readily neutralized *in vitro* by a variety of simple dissociable salts as well as by more complex substances, such as bacterial disintegration products, cholesterin, proteins, and organ extracts. There are also leukocytic poisons that may paralyze phagocytosis.

In human beings experience shows that overwork, depression, overcrowding and unhygienic living, chronic renal, hepatic, and cardiac lesions, diabetes, exanthematous and other acute and chronic infectious diseases, and sudden changes of temperature favor the development of general infections.

In the etiology of diseases like diphtheria and pneumonia, which are caused by bacteria that are disseminated widely even in the well, the factors that lower general resistance play a very important rôle.

It is not unlikely that various chronic diseases are associated with diminution in the amount of antibacterial substances normally present, but the conditions are in reality so complex that they cannot now be successfully analyzed.

In many chronic diseases and conditions of exhaustion the opportunities for local infections are increased greatly. It is generally believed that the *locus minoris resistentiæ* plays a decisive part in determining the localization of pathogenic bacteria that have entered the circulation and that ordinarily would be destroyed without doing any harm. Such favorable local conditions may be caused by injury, inflammation, and other previous diseases. The predisposing influence of injury in the lodgment of tubercle bacilli and pyogenic cocci in bones and joints is established both clinically and experimentally. Bacteria are much more likely to obtain a foothold on diseased than on normal heart-valves. The presence in the lungs of foreign particles of various kinds as well as of inflammatory processes favors the development of pulmonary tuberculosis.

The degree of resistance is also of influence upon the course and the character of infections. Of course, the relative virulence of the infecting organism must be considered in this connection. We have abundant evidence, however, to show that in animals many infections remain localized in the relatively resistant, whereas in the susceptible general invasion takes place. The differences in the course and character of tuberculosis and of pyogenic and pneumococcal infections in man are explainable in large measure by differences in susceptibility. Crushed tissue and hemorrhagic infiltrations at the point of entrance favor severe infections because the infecting agents here obtain favorable conditions for growth and increase in virulence.

The point of entrance is of great influence in many infections. This is well illustrated by the difference between staphylococcus and streptococcus infections of the subcutaneous tissue and of the leptomeninx or the peritoneum; though caused by the same organisms, these localizations differ very greatly as to course and termination.

The relative virulence of pathogenic organisms plays a most important part in infections. Virulence, by which we understand the degree of pathogenic power of an organism, depends on different properties. In some bacteria virulence in this sense is dependent upon their toxicogenic power, that is, the power to produce soluble, diffusible toxins, rather than on the power to invade the tissues. B. diphtheriæ and B. tetani are examples of this class.

In the case of many other bacteria virulence is locked up with invasiveness because the disease-producing substances are liberated only as the bacteria reach the interior of the infected body.

Generally speaking, virulence is a changeable quantity, being most marked when microbes are isolated from the infected body and gradually undergoing attenuation as cultivation on artificial media progresses. It is noteworthy that the invasive bacteria suffer reduction in virulence under artificial conditions much more quickly than the toxicogenic. In the case of several bacteria (streptococci, staphylococci, pneumococci) media containing blood or serum are useful in conserving virulence. Growth at temperatures higher than 37° C., exposure to sunlight, treatment with various chemicals, etc., have been found to reduce virulence quickly. Passage through animals of one species may result in increase of virulence for that species but loss of virulence for some other species. Thus, Knorr and Petruschky found that as streptococci were passed through rabbits they lost in virulence for mice. According to one view, the virulence of the virus of smallpox is reduced so as to make vaccine virus on passage through calves.

While high virulence for animals generally is thought to indicate virulence for man, this is probably not always the case. Thus streptococci highly virulent for rabbits may not produce erysipelas in man (Koch and Petruschky).

As a general rule, pathogenic bacteria commonly increase their virulence when successively inoculated into susceptible animals. In this way anthrax bacilli, streptococci, pneumococci, and cholera bacilli may reach a remarkably high degree of virulence, which gradually diminishes on continued artificial growth. Rosenow in our laboratory succeeded in increasing the virulence of a strain of pneumococcus isolated from the blood of a pneumonia patient, so that as nearly as could be estimated ten pneumococci sufficed to kill a full-grown rabbit in twenty-four hours. Observations of similar import have been made with reference to streptococci and anthrax bacilli.

There is good reason to believe that acute bacterial infections in man also lead to a more or less temporary increase of virulence of the bacteria concerned, and that this may be of great importance in the spread of diseases readily communicable from the sick to the susceptible, as in streptococcal angina and pneumonia.

When recently isolated, typhoid bacilli are more resistant to agglutination than after growing artificially for some time. Experimentally it has been found that on growth in immune antityphoid serum, which has been inactivated by heat, typhoid bacilli may grow in virulence and in resistance to agglutination (Walker, Edna Steinhardt and others). It is possible that in a measure this may be the outcome of the survival of the stronger, more resistant elements, but an actual increase in resistance to antibodies and in invasiveness cannot be wholly excluded. Following Pfeiffer and Kolle as well as others, Strong has demonstrated that the more virulent the cholera spirillum, the greater is the amount of substance (receptors) upon which antibodies must act. The same is true of the anthrax bacillus (Danyscz), and probably also other bacteria. In some cases, then, growth in virulence is associated with increase in bacterial receptors and in resistance to antibodies.

In the cases of streptococci, pneumococci, staphylococci, and probably also other pathogenic bacteria, increased virulence is associated with greatly increased resistance to phagocytosis as compared with feebly virulent and non-virulent strains (Denys, Hektoen and Ruediger[15]). Indeed, Marchand defined a virulent streptococcus as one that is more or less susceptible to phagocytosis. This insusceptibility to phagocytosis appears to depend upon a greatly increased resistance of the virulent cocci, even when killed by heat and washed, to the opsonic action of serum. In the case of animal-virulent streptococci, normal serum rarely contains sufficient opsonin to render the cocci fit for phagocytosis; immune antistreptococcus serum for animals injected with virulent streptococci, however, may contain enough opsonin to render the cocci suitable for the phagocytes (Neufeld and Rimpau).

Bacterial virulence has been explained as dependent upon the production of leukocytic poisons; and it has been shown that leukocidal substances are produced by virulent staphylococci (Van de Velde), by streptococci, and possibly also by pneumococci (Cassagrandi), and it lies near at hand to suppose that these poisons also may be an index of the invasive and resistive powers of the bacteria in question.

Recently it has been demonstrated that when sterilized bacterial exudates are injected together with the corresponding bacteria death ensues more quickly than when the bacteria are injected alone, and Bail assumes that the exudates contain certain specific bacterial derivatives that paralyze phagocytes and other means of defence. These substances have been called aggressins. It is, however, very likely that the exudates contain also many nonspecific bodies that may bind or absorb complement and opsonin, so that it is too early to accept the aggressin theory of virulence in its present form.

A few years ago Welch[13] advanced a general theory of bacterial virulence by applying to pathogenic bacteria Ehrlich's lateral-chain theory of the origin of antibodies in the host. According to Welch, there "is no reason why suitable substances derived from the host may not stimulate parasitic organisms, through a physiologic mechanism similar to that operative in cytolytic (bacteriolytic) immunity, to the production of intermediary bodies (amboceptors), which, if provided with requisite affinities, have the power to link complements to cellular constituents of the host, and thereby poison the latter." This theory of bacteriogenic antibodies would explain well the toxic power of many microbes that in artificial culture quickly lose virulence and give little indication of the production of poisons.

The interesting fact that in nature bacterial virulence remains at a comparatively low level is explained by Theobald Smith[16] as in full harmony with the fundamental biologic law of preservation of species. Many pathogenic germs have been reduced more or less completely to a parasitic existence, and in order to maintain the species an adaptation has taken or is taking place to conditions permitting invasion of host after host. Now, the more virulent the microbe, the more rapid the death of the host and the less the chance to pass to new hosts. In consequence there is going on in nature a gradual weeding out of the most virulently pathogenic parasitic microbes in favor of those better adapted to parasitism. Advancing parasitism results in a gradual decline in virulence and in mortality. In other cases where the continuation of the microbic species is dependent upon the continuation of the host species, there may have been, as suggested by Bayard Holmes for tuberculosis, leprosy, and syphilis, a low degree of initial virulence on the part of the parasites.

The Local and General Effects of Infection.—The local changes of infection are principally necrotic and inflammatory in nature, but owing to the variations in virulence and in susceptibility, and to differences in the tissues infected and in the manner of infection, the same organism may be the cause of anatomically different local lesions, the evolution and morphology of which are described elsewhere.

In general the local changes are caused by chemical substances of bacterial origin, and they do not necessarily depend upon the presence of living germs, as they may be produced by the injection of dead cultures and of sterile products of bacterial growth. Buchner showed that pathogenic as well as saprophytic bacteria contain proteins that in warm-blooded animals attract leukocytes and cause exudation from the vessels.

As the microörganisms multiply in the tissues more specific substances are liberated also, upon which probably depend the peculiarities characteristic of certain inflammatory reactions, but as yet these substances are not well understood.

It is at present accepted quite generally that the inflammatory reaction, resulting, as it does, in the concentration of leukocytes and of serum about the microörganisms, serves to protect the body and to promote healing. In addition to the local accumulation of antibodies such as opsonins and bacteriolysins normally present in the blood, it is also not unlikely that there may be a local production of specific antibodies that further healing.

Most infections, and especially those of peculiar interest to the surgeon, give rise to leukocytosis, the increase being chiefly in the polymorphonuclear neutrophile forms. The leukocytes probably make their way into the blood from the marrow by their amœboid motion and in response to positively chemotactic substances.

In animals experimental infections are commonly marked by an initial hypoleukocytosis, but in man infections establish themselves far more gradually, and an initial hypoleukocytosis is not so constant or so marked as in animals. This hypoleukocytosis has been explained as the result of an unequal distribution of the leukocytes, which are held back in large numbers in the internal organs. As the positively chemotactic substances diffuse more uniformly, the white cells become distributed more equally in all parts of the blood; and in the meantime the bone-marrow is stimulated to an increased production of neutrophile myelocytes.

In some infections there is a permanent leukopenia so long as they remain uncomplicated. This is the case in typhoid fever, measles, rötheln, malaria, dengue, uncomplicated tuberculosis except of serous surfaces, and some forms of general sepsis. In these infections we assume the presence of negatively chemotactic substances or at least the absence of positively chemotactic influences.

Infectious leukocytosis must be regarded as beneficial to the infected body for various reasons. In the first place, the production of new leukocytes in the bone-marrow compensates for the loss of leukocytes in inflammatory exudates and suppuration. Leukocytes are regarded as one of the sources of antitoxic and bactericidal substances; recently Pettersson has extracted from dog leukocytes a heat-stable, anthracidal substance; and leukocytes furnish by far the largest number of phagocytes, not only for destruction of bacteria, but also for removal of cellular detritus of various kinds. In the test-tube it is easy to show that the destruction of certain bacteria by phagocytosis (streptococci and pneumococci and human leukocytes, anthrax bacilli and dog leukocytes) is greater the larger the number of available leukocytes. The leukocytes of experimental and infectious leukocytosis seem in general to be quite as active in this respect as the leukocytes of normal blood. The undoubted increase in local and general resistance following the increase of leukocytosis by the injection of various substances—nucleinic acid, serum, broth, salt solution—also testifies to the protective power of leukocytosis. Various authors have concluded that the pre-operative production of a peritoneal leukocytosis protects patients from infection.

Some pathogenic bacteria produce toxins that lake red blood-corpuscles (hemolysins), and these no doubt play an important part in causing the anemia of many infections. All pathogenic staphylococci produce a substance of this kind, first observed by Van der Velde, and subsequently studied fully by Neisser and Wechsberg, who named it staphylolysin. Normal human blood contains antistaphylolysin, which is increased manifold in the course of staphylococcus infections, and it has been proposed to take advantage of this increase for diagnostic purposes in obscure cases of suspected staphylococcus infection.

In severe streptococcemia laking may occur, and Besredka demonstrated that virulent streptococci produce a lysin (streptolysin) which G. F. Ruediger[16] showed possesses the constitution of a toxin. The diffuse red staining of the endocardium and the intima of the aorta, long noted in cases of severe sepsis, may now be referred to laking of the blood by bacteriolysins, especially staphylolysin and streptolysin. Crude tetanus poison contains a typical lysin (Ehrlich and Madsen) which gives rise to an antilysin when injected into certain animals.

Recently the hyaline thrombi that occur in infections have been traced to the agglutination of red cells by hemo-agglutinins of bacterial origin (Flexner).

In typhoid fever, scarlet fever, and other infectious diseases there occurs a marked leukocytosis and disintegration of red corpuscles by leukocytes and endothelial cells in the spleen, lymph and hemolymph nodes, and vessels. The exact mechanism of this phagocytosis has not been unraveled, but it may be that substances are elaborated that make the red corpuscles susceptible to phagocytosis by homologous leukocytes (hemopsonins). As a matter of fact I have found recently that the serum of patients with various infectious diseases—*e. g.*, typhoid fever, pneumonia, scarlet fever, erysipelas—contains substances that lead to phagocytosis of human red corpuscles by human leukocytes.

The enlargement of the spleen in various infections depends in part upon the lodgment therein of disintegrating red corpuscles, which are taken up freely by cells in the pulp. At the same time there is hyperemia and cell proliferation. Pfeiffer and Marx have brought this hyperplasia into relation with the elaboration of specific antibodies especially in typhoid fever.

The marrow commonly shows an increase in neutrophile myelocytes, the mother cell of the neutrophile leukocyte. Here as well as in the lymph and hemolymph nodes phagocytosis of red cells and leukocytes occurs, associated with more or less endothelial proliferation. According to Warthin,[18] the hemolymph nodes may show greater phagocytic activity than the spleen.

Many pathogenic organisms and their poisons have a special affinity for the nervous system, as illustrated by leprosy, hydrophobia, tetanus, diphtheria, and the toxin of B. botulinus. It has been shown that tetanospasmin reaches the nerve-cells by way of the axones. The particular constituent of the crude diphtheria toxin that causes neuritis and paralysis is called by Ehrlich toxone. It has been shown experimentally that numerous common pathogenic bacteria directly or indirectly may induce grave changes in the spinal cord; this is illustrated by the clinical relations between myelitis and various infectious diseases.

The exact investigations of the influences of microbic poisons upon various glandular functions and upon the circulatory apparatus are not yet far advanced. It has been found that diphtheria toxin lowers the power of adrenal extracts to raise blood-pressure. In experimental pneumococcus-, pyocyaneus-, and diphtheria-infection vasomotor paralysis is given as the real cause of heart failure by Paesser and Romberg.

Diphtheria- and tetanus-toxin have been found in the urine of patients with the respective diseases; the general toxicity of the urine in infectious diseases was claimed to be greatly increased by Bouchard, but the subject needs further study.

The exact mechanism of the production of the parenchymatous degenerations of injections, whether the result of hyperthermia alone or of the more direct action of microbic products, has not been settled definitely.

Fever is a constant accompaniment of active infection, and it has been demonstrated conclusively that the introduction of suitable quantities of living or dead infectious material generally causes rise of temperature. The various fever-producing substances that have been isolated from bacteria do not so far appear to differ from derivatives of other kinds of protoplasm that cause fever when injected. The many definite types of fever curves—continuous, remittent, etc.—would appear to indicate that there is no single thermogenic substance or agency common to pathogenic microbes; we know that secondary streptococcus infection in pulmonary tuberculosis causes a change in the type of fever; at all events, the manner of production of the pyrogenic substances differs in different infections. In some infections the fever type stands in definite relations to the development of specific microbic substances. In recurrent fever, for instance, the fall of the temperature corresponds to the appearance of antibodies that check the growth of the spirilla. There is also reason to believe that in pneumonia the crisis with the fall of temperature depends on the sudden development of pneumococcidal substances.

From animal and human experiments it has been learned that the reactions causing the various antibodies—antitoxins, lysins, agglutinins—are associated with fever which appears to be essential for the formation of the new substances. The injection of excessive quantities of antigenic substances may cause fall of temperature and general collapse; hence it may be that the subnormal temperature in very severe infections, and the absence of fever in some infections in the aged, is due to a paralysis of the usual cellular reactions. At present there is a tendency to look upon fever not as harmful *per se*, but rather as beneficial in so far as it may be regarded as an indication that certain reactions essential to the natural healing of infections are taking place. Experiments calculated to show the effect of pyrexia alone upon experimental infections with various bacteria have not given decisive results applicable to spontaneous infections. When pyrexia is induced by the Sachs-Aronson puncture shortly before or soon after the injection of the bacteria, streptococcus, pneumococcus, and anthrax infections appear to be withstood better than in the control animals. This may be due to increase in general resistance.

IMMUNITY, THE FORMATION OF ANTIBODIES, AND SERUM THERAPY.

For centuries it has been known that recovery from infection in many cases leaves behind a more or less pronounced specific immunity, which more recent investigations have shown to be closely associated with certain cellular reactions that result in a variety of bodies, called antibodies, which, like antitoxins, may neutralize microbic toxins, or, like the lysins and opsonins, destroy or promote the destruction of microbes, while others cause agglutination and precipitation.

The Origin of Antitoxins and Other Antibodies.—Under suitable conditions toxins and other substances induce in the animal organism the formation of specific antibodies. Substances having this power may be called antigens, of which we have become acquainted with several during recent years.

Toxins were the first antigens studied, and their mode of action was described somewhat as follows by Ehrlich[10] in the celebrated lateral-chain or receptor theory of immunity. Toxins are harmful only after uniting with free atomic groups or side chains, also called receptors, in the cell molecules. If a cell contains no receptors with which to hold fast the toxin molecule, then that cell is naturally immune to the toxin, and it has been found that in immune animals certain toxins may remain free, unaltered for a long time, whereas in susceptible animals the toxin quickly becomes bound. Nerve-cells, for instance, have a marked affinity for tetanus toxin (Wassermann and Takaki), and red corpuscles take up from mixtures specific toxins that produce laking.

In addition to the group by means of which toxin molecules link themselves to all receptors, Ehrlich postulated a second group, through which the toxic effect is produced because on standing and other treatment toxins may become harmless and nevertheless have the power to unite with cells. The first group has been called the haptophore or cytophile group and the second the toxophore group.* Evidently the toxophore or functional group is much the more sensitive of the two groups, and toxins that have lost the toxophore group are called toxoids.† The haptophore group may be active at a temperature at which the toxic group remains inactive, as in frogs, in which tetanotoxin is not toxic below 20°C., even though bound to the nerve-cells.

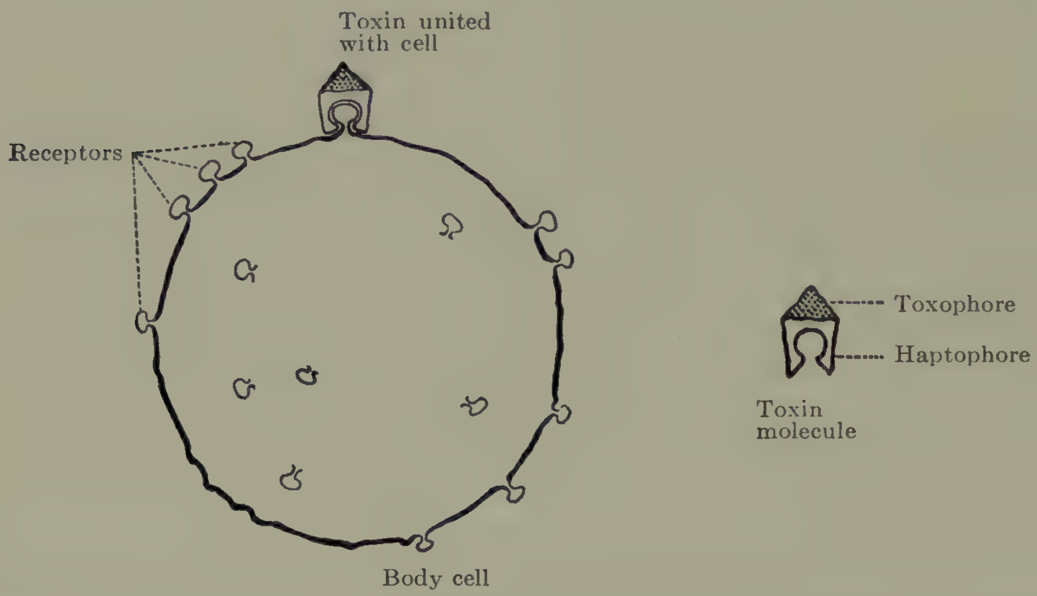

Fig. 32.—The Mechanism of the Toxin-cell Union by the Intermediation of Receptors (Da Costa).

The production of antitoxins is referred to by Ehrlich as an illustration of Weigert's law of regenerative over-compensation. When the side chains or receptors of a cell are so occupied by toxin (or other antigen) that cellular metabolism suffers, a new production of receptors is initiated that exceeds the immediate needs of the cell, and the excess of receptors is thrown off into the circulation as free antibodies. Hence, theoretically, any cell that can bind antigens and produce receptors is capable of producing free antibodies. There are good grounds for believing that antitoxins may be formed in various parts of the body. Römer and others have observed their development *in loco* where antigens are introduced, and leukocytes are thought to be able to produce various antibodies.

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* In the case of antigens without direct toxic action the analogue of the toxophore group is called the functional or zymophore group.

† Other antigens are also susceptible of this "oid" transformation.

According to Ehrlich's theory, then, antitoxins are free cellular receptors, and there are a number of other antibodies the formation of which is susceptible of the same explanation, the particular kind of receptor set free depending upon the antigen that sets in motion the mechanism of receptor regeneration. By gradual stimulation of this mechanism by injection with increasing quantities of antigen large amounts of antibody may accumulate in the blood, as illustrated so well in the immunization of horses to diphtheria and tetanus toxins.

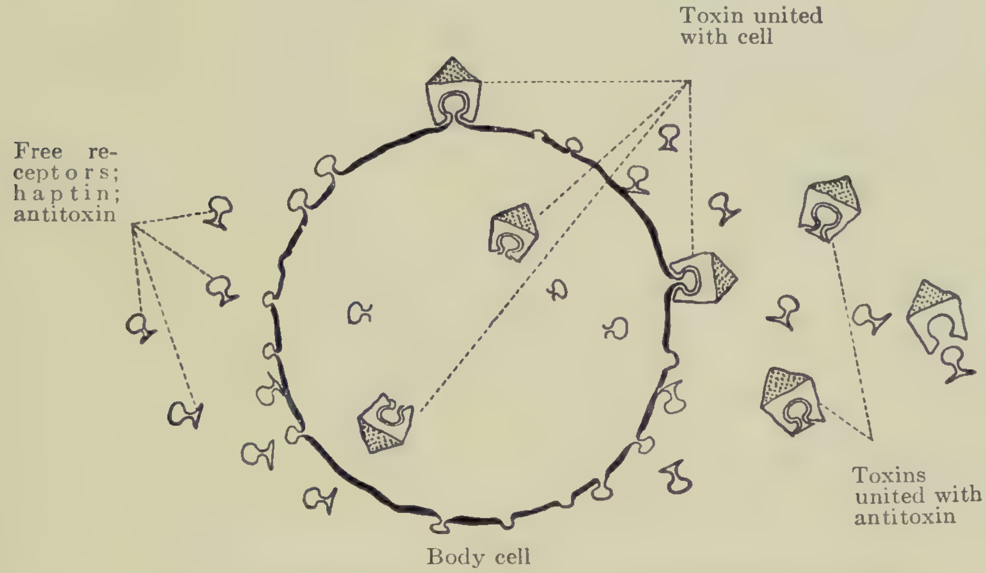
Toxin united with cell
Free receptors; haptin; antitoxin
Toxins united with antitoxin
Body cell

FIG. 33.—THE ELABORATION AND ACTION OF ANTITOXIN (Da Costa).

Ehrlich and others have shown that antitoxins and other antibodies are transmitted from the maternal circulation to the offspring, and after birth to a less extent through the milk, thus producing in the offspring a degree of passive immunity which, however, is of brief duration.

The following table gives the antigens and antibodies best known at this time:

ANTIGENS AND ANTIBODIES.

ANTIGENS. (IMMUNIZING SUBSTANCES.)	ANTIBODIES. (PRODUCTS OF IMMUNIZATION.)
Toxins	Antitoxins
Ferments	Antiferments
Precipitinogens	Precipitins
Agglutinogens	Agglutinins
Opsogens	Opsonins
Lysogens (amboceptorgens)	Amboceptors (lysins)
Antitoxins	Antiantitoxins
Agglutinins	Antiagglutinins
Complements	Anticomplements
Opsonins	Antiopsonins (?)
Amboceptors	Antiamboceptors
Precipitins	Antiprecipitins

Antitoxins.—We owe the discovery of antitoxins to Behring,[20] who, in 1890, found that the serum of animals injected with increasing quantities of diphtheria toxin contains a specific antitoxic substance. Almost simultaneously analogous observations were made in regard to tetanus toxin (Behring and Kitasato) and to the vegetable toxins, ricin and abrin (Ehrlich). Then followed the demonstration that antitoxic serum not only protects healthy animals against fatal doses of the corresponding toxin, but even cures those already sick. Curative serum therapy was established.

Antitoxins are conceived to be free cell receptors. They are protective and curative because they unite with the toxin and prevent it from causing disease by uniting with cells. Large doses of antitoxin may break up recent combinations between cells and toxin, but as time goes on this union becomes firmer and firmer, and antitoxin may be able no longer to arrest toxin action. It is upon the free and very recently attached toxin that antitoxin acts, and for this reason it is imperative that large quantities of antitoxin should be administered early in toxic infections like diphtheria and tetanus.

Not all animals influenced by a certain toxin respond equally well by antitoxin production. Guinea-pigs, for instance, can be immunized to diphtheria and tetanus toxins by means of artificially weakened toxins. On a large scale therapeutic antitoxic serum is produced by subcutaneous injections with increasing quantities of toxin in healthy horses, great care being used that a moderate degree only of general reaction is set up and that the reaction is allowed to come to an end before new injections are made.

The sera of all immunized animals do not possess the same antitoxic value, and consequently therapeutic sera must be standardized carefully. At present antidiphtheria serum is the only official therapeutic serum in this country, and the method of standardization is by law established by the United States Public Health and Marine Hospital Service,[21] which also has in hand the preparation of a much-needed American standard for antitetanus serum. It is self-evident that progress in practical serum therapy must depend on the use of sera of ascertained strength, so that the results attained may be comparable.

We know but little concerning antitoxins outside of their specific actions. They are weakened or destroyed by light and by heating at 60° to 70° C.; when dry they tolerate heat better and keep longer. Atkinson found that in fractional precipitation of antitoxic serum diphtheria antitoxin is carried down by the globulin.

The possibility that antitoxins and other immune bodies exist as purely colloid substances and owe their actions to being in a colloid state is now receiving attention (see analogy between precipitation of colloids and agglutination and specific precipitation, page 178).

The explanation of antitoxic action at first was largely vitalistic, but all views of this kind were abandoned when it was found that antitoxins act *in vitro* as well as *in vivo*, and that in a number of instances toxic and antitoxic action may take place without the immediate coöperation of the living organism, as, for instance, in the case of certain blood-laking toxins of bacterial origin and their antitoxins (tetanolysin, staphylolysin, and others). Here washed red corpuscles are used as indicators, the laking being measured readily by colorimetric scales.

The rapidity with which toxin and antitoxin unite has been shown to depend on the degree of concentration, the temperature, the medium, the amount of salts present, etc.

Ehrlich soon found that there is no fixed relation between the toxicity of crude diphtheria toxin (soluble products in filtrate of broth cultures) and its power to neutralize diphtheria antitoxin. Various influences—time, heat, light, etc.—reduced the toxicity without altering the power to neutralize antitoxin. Evidently the crude diphtheria poison may contain substances that are non-toxic and yet have as great or even greater avidity for antitoxin as the toxin proper. Ehrlich has called these substances toxoids. Toxoids are toxins that have no toxophore groups.

Ehrlich's explanation of the fact just cited has been accepted generally. His claim that diphtheria poison contains two active toxins, the diphtheria toxin proper and toxone, the latter being the body that is held accountable for the late paralysis in diphtheria, has been attacked by Arrhenius and Madsen. The Scandinavian investigators hold that the reactions between toxin and antitoxin are reversible, analogous to the reaction between substances of feeble affinity, and hence following the Guldberg-Waage law of mass of action. Ehrlich and his supporters insist, however, that the mixtures are not homogeneous and that the degree of reversibility, if any exists, is extremely limited. At present Ehrlich's conception of toxin and toxone seems to have the larger following.[22]

The early expectation that it would be an easy matter to obtain specific sera against all microbic diseases by following the scheme for obtaining antidiphtheria and antitetanus sera was doomed to disappointment. Most infectious bacteria do not owe their morbific power wholly to diffusible toxins, and it has been recognized that acquired antitoxic immunity, which depends essentially upon the chemical neutralization of pathogenic toxin by antitoxin, has only a limited range. In human pathology diphtheria and tetanus are the only two diseases in which antitoxins play the principal rôle in spontaneous healing and in which curative serum therapy has achieved decided results.

Lysins.—Bacteriolysis, *i. e.*, the solution of bacteria by serum, is a somewhat complex process. While Nuttall and others brought definite proof of the bactericidal action of normal defibrinated blood and other fluids, and while Nissen, v. Behring, and Bouchard showed that immunization with certain bacteria greatly increased the bactericidal power of serum, the finer mechanism of this destruction remained, obscure until attention became directed to the so-called "Pfeiffer's phenomenon." R. Pfeiffer observed that cholera germs placed in the peritoneal cavity of a guinea-pig immunized to cholera undergo solution. Soon typhoid, pest, and other bacteria were found to suffer a similar fate under analogous conditions. The microörganisms become immovable, swell up, and form balls that gradually melt away. In many cases phagocytosis takes place at the same time, especially when destruction is slow.

The specific nature of this destruction was noticed from the first, and Pfeiffer showed that lysis occurs in the abdomen of a normal guinea-pig provided specific immune serum is introduced. Metchnikoff and Bordet soon demonstrated that specific bacteriolysis takes place *in vitro* also.

The discovery by Bordet that injections of alien red corpuscles give rise to antibodies or lysins that lake the kind of corpuscles injected promoted greatly the study of bacteriolysis and placed in the hands of Ehrlich and his co-workers a convenient material for exhaustive investigation. The fact that normal serum may lake alien corpuscles was known already, and it soon became known that hemolysis as well as bacteriolysis by the serum of normal and of immune animals depend upon analogous factors and follow similar laws. By immunization, *i. e.*, repeated injections of animal and bacterial cells as well as cellular disintegration products, the amount of specific lytic substance may be greatly increased or entirely new lysins produced in a specific manner. The cellular constituents that give rise to lysins have been called lysogens.

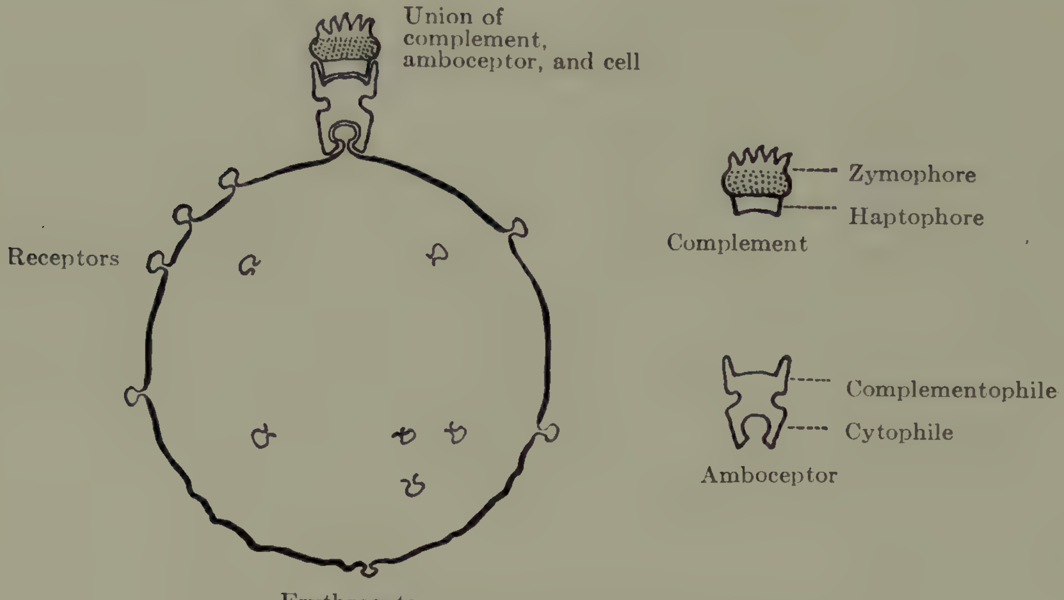

FIG. 34.—THE MECHANISM OF HEMOLYSIS (Da Costa).

Normal as well as immune lytic serum owes its lytic power to the presence of two interacting bodies: (*a*) one that, as a rule, is destroyed by heating the serum at 55° C. for thirty minutes, the complement, which is normally present in the blood and is not increased by immunization; and (*b*) one called amboceptor or immune body that is more thermo-stable and is increased specifically or produced anew on immunization, as the result, according to Ehrlich's theory, of an overproduction of cell receptors. Serum that has lost its lytic power from destruction of the complement by heat or otherwise is said to have been inactivated; it may be reactivated by adding fresh serum containing complement.

As the name indicates, amboceptors differ from antitoxins in having two binding or haptophore groups, one by means of which they are attached to the cells, the cytophile group, and one by means of which the complement is linked to the cell, the complementophile group. Alone the amboceptor is not destructive of cells, bacterial or otherwise; the destruction or laking, as the case may be, is always accomplished by the complement after it becomes attached to the cell by the amboceptor.

Amboceptors are quite stable bodies; heating at 60° C. for several hours has no appreciable effect upon them, but heating to 70° C. for one hour destroys them.* The same serum may contain more than one amboceptor, and the amboceptors in different sera usually differ in their cytophile or complementophile groups or both. A serum may contain an amboceptor for a given cell, but not any suitable complement. This is the case with dog serum, which contains an amboceptor for anthrax bacilli but no complement; rabbit serum contains the particular complement necessary in this case.

Flexner and Noguchi [23] demonstrated that the marked cytolytic action of snake venoms is due to amboceptors that unite with the cells and then with the normal complements of the blood, thus turning a defensive agent against the cells of its own body. Kyes[24] found that lecithin may complement the hemolytic amboceptor of cobra venom, thereby putting a known chemical substance in the place of the unknown complement.

The rôle of cellular constituents in causing new amboceptors is shown very clearly by the fact that when animals are injected with corpuscles or bacteria that have been treated with inactivated immune serum no new production of amboceptors ensues, because, the side chains of the injected cells being occupied, they cannot unite with the side chains or receptors of the animal injected and so start the formation of new receptors (amboceptors). Conradi, Neisser, Shiga, Strong, and others have shown that autolysis of killed bacteria (dysentery, typhoid, cholera) sets free receptors—lysigens—which give rise to immune bodies, and various "vaccines" prepared along this line are now used for protective inoculations, causing an active anti-infectious immunity of shorter or longer duration.

Complements are sensitive substances often likened to ferments. The same blood may contain different complements, and the complements in different bloods may vary, especially as regards their haptophore groups. Complements generally are neutralized by a variety of simple salts ($CaCl_2$, $Na_2C_2O_4$, $Na_3C_6H_5O_7$, etc.). They resemble toxins in having two groups, one haptophore and one toxophore or zymotic. The toxophore group may be inactivated in various ways, while the haptophore remains intact and able to unite with the amboceptor (complementoid). On injection serum containing complement or complementoids may give rise to anticomplements, and inasmuch as anticomplements are obtained by injection of washed leukocytes also, these have been regarded as a source of complements.

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*Certain normal and immune sera contain thermo-stable bactericidal substances, the exact nature of which, whether simple or complex, has not been determined definitely. Alice Hamilton and Jessie Horton have found that the serum of animals immunized against certain pseudodiphtheria bacilli contain a specific bactericidal substance that withstands heating at 88° C. for one hour. The anthracidal action of normal rat serum depends probably on a similar substance.

There are many important details concerning complements and amboceptors that cannot be discussed now—such as the formation of antiamboceptors and the so-called deviation of complement in the presence of excess of free amboceptors.

Acquired immunity, natural as well as artificial, against typhoid, cholera, dysentery, and certain other bacteria, is associated with the appearance of newly formed, specific, bacteriolytic immune bodies or amboceptors, and for this reason the immunity in these instances has been spoken of as antibacterial or bacteriolytic in nature. The therapeutic use of bacteriolytic serum has not given the desired results, except possibly in dysentery. On the other hand, the production of an acquired active immunity by the inoculation of heated bacteria and of bacterial disintegration products appears to render considerable protection to spontaneous infections. This acquired immunity may depend upon the fact that bacteriolysis is so accelerated that the bacteria are destroyed before they have multiplied sufficiently to produce on disintegration appreciable quantities of endotoxin. The relative immunity that seems to persist for a time after the bacteriolytic substances have passed out of the blood has been ascribed to an abnormal sensitiveness of the cells, which now react with great promptness, setting free on slight stimulus abundant antibodies.

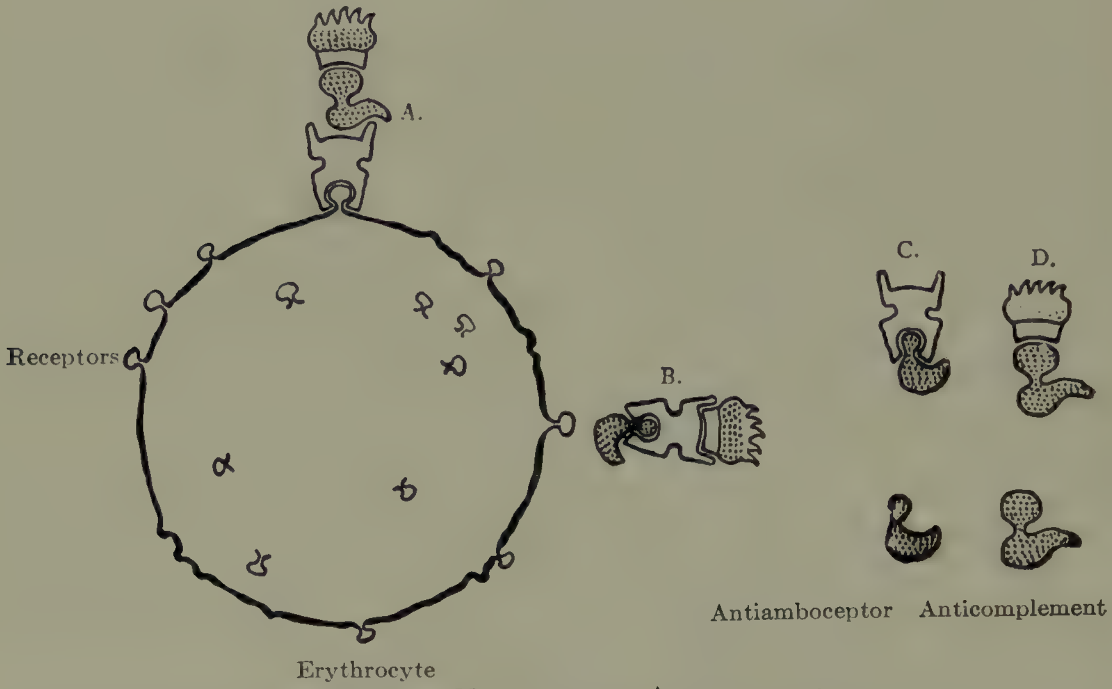

FIG. 35.—THE MECHANISM OF ANTIHEMOLYSIS.

A, Interference of anticomplement with complement-ambocepter union; B, interference of antiamboceptor with amboceptor-cell union; C, antiamboceptor-amboceptor union; D, anticomplement-complement union (Da Costa).

Opsonins (Phagocytosis).—Normal blood of man and of various animals contains substances that render bacteria susceptible to phagocytosis. These substances have been called opsonins (from the Latin *opsono*, "I cater for," "I prepare food for") by their discoverers, Wright and Douglas.[25]

It has been shown that bacteria suspended in salt solution are not taken up by leukocytes freed from serum by repeated washing in NaCl solution. When mixed with opsonic serum, various bacteria take up opsonin, so that they remain fit for phagocytosis after all the serum is removed by washing and such sensitized bacteria are not recognizably altered otherwise in form or function.

Normal opsonins are rendered inactive by heating at 54° to 60° C. for thirty minutes, some being more resistant to heat than others. They resemble complements not only as regards their feeble resistance to heat, but also in being bound or neutralized by numerous salt solutions like $CaCl_2$, K_2SO_4, $Na_3C_6H_5O_7$, $K_4Fe(CN)_6$, etc., as well as by formalin and lactic acid.[15] The opsonins in the blood of one species may prepare some bacteria for phagocytosis by heterologous leukocytes. Normal human serum contains opsonins for staphylococci, streptococci, avirulent pneumococci, meningococci, typhoid bacilli, anthrax bacilli, tubercle bacilli, diphtheria bacilli, and probably many other bacteria.

Nothing definite can be said as yet concerning the mechanism of opsonic action, which in some way substitutes a positive for a negative chemotaxis between the leukocytes and the bacteria. Even when the leukocytes are paralyzed or killed by heating to 45° C. pneumococci may gather about them in large masses, provided that opsonic serum is present.*

Like other antibodies, opsonins are increased in a specific manner as the result of infections and experimental immunization. Before the recognition of opsonins and opsonification, Denys and his co-workers as well as others observed that virulent streptococci were taken up by rabbit leukocytes only in the presence of an immune antistreptococcus serum. Analogous observations were made by Mennes with respect to pneumococci, and by others with respect to other bacteria and the respective immune sera. These phenomena were interpreted, however, as due to a special stimulation of the phagocytes. But Neufeld and Rimpau[26] pointed out (independently of the observations of Wright and Douglas) that it is the virulent streptococci and pneumococci that take up certain substances (termed by them bacteriotropic substances) from the specific immune serum and not the leukocytes. The immune serum so changes the corresponding bacteria that normal leukocytes ingest them. Wright and Douglas found the opsonic power of the serum greatly increased in cases of chronic staphylococcal furunculosis after injections of 0.75 to 1 c.c. of a heated broth culture of staphylococci. The analogous result followed the injection of a tubercle vaccine in cases of tuberculosis. Neufeld and Töpfer[27] found that the serum of rabbits immunized with goat blood developed a specific substance that rendered goat corpuscles susceptible to phagocytosis by guinea-pig leukocytes.

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* Unpublished observation by Dr. Rosenow in our laboratory.

Immunization of other animals with alien blood also gives rise to specific opsonins (Barratt, Hektoen). These immune opsonins (hemopsonins) are different from lysin and from agglutinin because these may be present in serum without having any opsonic effect.

There is little reason to doubt that phagocytosis is essential for the destruction of certain bacteria in mixtures of leukocytes and serum. Denys showed that destruction of virulent streptococci in mixtures of rabbit leukocytes and immune serum was associated with an active phagocytosis, while serum alone and phagocytes alone had little or no effect. G. F. Ruediger[28] has found that normal defibrinated human blood has some streptococcidal effect, and that blood from patients with an infectious leukocytosis has a greater destructive effect, which is in proportion to the number of leukocytes, but that fresh serum, in itself non-streptococcidal, must be present. Anthrax bacilli grow freely in dog serum, but are destroyed readily in defibrinated dog blood, and this destruction is associated with marked phagocytosis and is in proportion to the number of leukocytes present. The opsonin for anthrax bacilli in dog serum is destroyed by heat at 60° to 62° C.

The pronounced and prompt phagocytosis noted by many observers in the peritoneal cavity in the presence of specific immune serum indicates that opsonins probably play the same part *in vivo* as *in vitro*. At present the production of opsonins is best explained in the terms of Ehrlich's lateral-chain theory.

Precipitins and Specific Precipitation.—Specific precipitins result from the injection into animals of various protein substances of animal, vegetable; or bacterial nature (zoö-precipitins, phyto-precipitins, and bacterio-precipitins). Kraus, of Vienna, first observed that cholera, plague, and typhoid antisera form precipitates with the corresponding bacterial filtrates. Tschistowitsch and Bordet found that serum of an animal injected with the serum of another species forms precipitate when mixed with the alien serum.

In man and in animals it has been demonstrated that precipitable substances or precipitinogens are present in the blood, the organs, in milk (Fisch), and in various pathologic fluids. Extracts of bacterial cultures and filtrates of broth cultures in many cases contain precipitinogen. The efforts to obtain these substances in pure form have not given final results as yet. Albumoses from flours contain precipitinogen (Kowarski). It is agreed, however, that precipitinogen is part of a proteid molecule possessing considerable resistance to heat, to alcohol, ether, decomposition and digestive enzymes.

Animals do not form precipitins against their own proteins and closely related animals do not readily produce precipitins for the sera of one another.

Precipitins are salted out with the euglobulin in fractional precipitation with ammonium sulphate, but further purification has not succeeded. It has been shown that precipitin contains two groups, one whereby it attaches itself to the precipitable substance and one that causes the precipitation. The functional group is destroyed by heating at 58° to 60° C. in bacterio-precipitin and at 70° in lacto-precipitin. When dry, precipitin withstands a much higher temperature. Precipitin that has lost its precipitating power is called precipitoid, and precipitoid may bind the precipitable substance with greater affinity even than does precipitin.

The precipitate that forms on mixing precipitin and the corresponding precipitonogen is insoluble in mineral salts, in soda, and resists digestion.

The formation of specific precipitates in the living body has been suggested as the cause, at least in part, of the untoward effects that sometimes follow the injection of therapeutic sera of animal origin.

The rapid disappearance of antitoxins as well as lysins from the blood of immunized animals and persons is explained as due, in part at least, to the formation from the injection of heterologous serum of precipitins giving rise to precipitates that carry down the specific antibodies. This is in accord with Behring's observation that in horses passive immunity lasts longer when produced by the injection of homologous than of heterologous antitetanus serum.

As in the case of agglutination, immune precipitin acts most strongly on the antigen employed to induce its formation, but in larger doses there may be some action also on related precipitinogens (group reactions). Thus Norris[29] shows that the sera of rabbits immunized with four representatives of the colon typhoid groups precipitated filtrates of all the members of this group tested, but quicker in homologous filtrates, and in high dilutions only in the latter. Serum precipitins are also specific, but on account of the number of precipitinogens in a serum the serum of immunized animals may contain a number of precipitins, the specificness of the main precipitin being demonstrable by increasing dilutions. Wassermann and Schütze and Uhlenhuth applied specific precipitation to the differential diagnosis of human and animal blood and albumins, and this test is now used in forensic medicine. Nuttall [30] has made comprehensive studies into the biologic relationships of animal species by means of specific precipitins.

Agglutinins and Agglutination.—Agglutinins are antibodies that cause particles in homogeneous suspension, *e. g.*, bacteria and corpuscles, to draw together into clumps. The serum that causes strongest clumping of a given bacterium is that of an animal immunized or of a human patient infected with this bacterium. Immediately after the discovery of specific agglutination by Gruber and Durham, Grünbaum and Widal applied agglutination to the diagnosis of typhoid fever, and the test has been extended to other diseases and also to the identification of bacteria suspected of causing infections.

Hemagglutinins occur in normal alien sera and in animals injected with corpuscles of another species; also in toxic substances of plant, animal, and bacterial nature. The hyaline thrombi in infections have been interpreted as probably due to agglutinins of bacterial origin (Flexner).

The power to induce agglutinins to form in the animal body is possessed in high degree by the bacteria of typhoid fever, plague, glanders, dysentery, and cholera, by the colon and paratyphoid bacilli, etc., but the Bacillus mucosus capsulatus group is poor in agglutinogens, which is the name given to the bacterial receptors concerned. When attached to the bacterial cells these receptors constitute the part with which the agglutinins unite.

The agglutinability of a given bacterium may vary from time to time and the same bacterium may produce more than one agglutinin. Theobald Smith and Reagh[17] found that motile bacteria may give rise to agglutinins that act on the bodies proper of the bacteria and to others that act on the flagella. Immune serum may therefore agglutinate bacteria closely related to the homologous organism (group agglutination), but the agglutinin for the homologous organism is present in the largest amount, and this agglutinin is called the chief agglutinin, in distinction to the common or adventitious agglutinins. Occasionally the common agglutinins may equal or even exceed the specific in amount. Inasmuch as agglutination is accomplished with the absorption from the serum of the agglutinin concerned, it is possible by selective absorption experiments to differentiate between the various agglutinins that may be present in the same serum.

Theoretically agglutinins may be conceived as free receptors with two groups, one by which they unite with the bacteria and one that causes the clumping (haptophore and zymophore groups). The zymophore group is destroyed by heating to 60° to 80° C., by treatment with acids and alkalies, and on long standing of the serum. The agglutinin is transformed into agglutinoid, and the agglutinoids, by occupying the bacterial receptors, may prevent agglutination on the addition of intact agglutinin. On fractional distillation the agglutinins are carried down with the globulins; agglutinins resist the action of pepsin and papayotin, but not of trypsin when prolonged.

The ability of the animal organism to form agglutinins varies considerably. Typhoid serum capable of agglutinating typhoid bacilli in a dilution of 1:1,000,000 was described by Van de Velde. It has been shown conclusively that the agglutinating and bacteriolytic substances are entirely different and distinct.

Gruber and others explained agglutination as due to an increased viscidity of the bacteria, and Paltauf advanced the idea that the bacteria became sticky because a precipitate formed on them. Bordet likened agglutination to the precipitation of a colloid suspension, and this explanation has received strong support from recent investigations by Bechhold and others.[31] Actual agglutination occurs after the agglutinin has united with the bacteria, forming the so-called agglutinin-bacteria, which now are drawn into clumps and settle down, provided salts are present (Joos). It is believed now that the same laws govern agglutination as govern the precipitation of colloid and other suspensions by salts, the basic element or cation* of which neutralizes the negative electricity of the suspended particles with the formation of clumps. In the case of bacterial agglutination the function of the agglutinin is believed to be the reduction of the amount of negative electricity carried by the bacteria, so that they become more susceptible to the action of the cations of the salts present. The explanation of specific precipitation would be quite the same as the one just given; here it concerns smaller particles.

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* *i. e.*, the ions going to the cathode.

CLASSIFICATION OF SERO-THERAPEUTIC METHODS.

The various sero-therapeutic methods have been classified as follows:

I. Protective Inoculations.—(A) **Active Immunization with Infectious Organisms.**—1. Injection of living, virulent organisms.

This method is illustrated by variolation, formerly practised in China and elsewhere. It is used even now in inoculation against sheep-pox; one disadvantage is that the inoculated disease, though milder than the spontaneous, may give rise to virulent epidemics. Young cattle may be immunized to Texas fever by the injection of the blood of animals that a few weeks previously passed through an attack and in the blood of which there are only few organisms. Normal animals are immunized to rinderpest by subcutaneous injection of bile of animals dead of the disease (Koch, Kolle). Ferran's anticholera inoculations are made subcutaneously with living cholera germs, which when so injected are quite harmless; the local reaction, however, is quite painful.

2. Injection of living, attenuated organisms.—The classic example is vaccination, discovered by Jenner in 1798, the smallpox virus being attenuated for man by passage through cattle. The successful immunization of cattle to tuberculosis by means of injections of the bacilli of human tuberculosis (McFadyean, Behring, Pearson and Gilliland, Koch) has been interpreted to this effect, that the human bacillus has become attenuated for cattle by passage through man, the bacilli of human and bovine tuberculosis originally being of the same kind. As early as 1881 vaccines were prepared by Pasteur against anthrax and symptomatic anthrax by growing the bacilli at 42° C. Pasteur's anti-rabies vaccines are secured by drying the spinal cords of rabbits that have died of injections with fixed virus.

3. Injections of dead organisms.—This method is employed in protective inoculations against typhoid fever, cholera, pest, dysentery. Pasteur's first vaccine against hydrophobia probably contains killed virus. In the bacterial diseases just mentioned protection is secured by the injection of dead bacteria, killed by heat usually, or of bacterial disintegration products the result of self-digestion and other processes. The degree of active bacteriolytic immunity produced in this way may be measured by determining the specific bacteriolytic powers of the serum.

(B) **Active and Passive Immunization Combined.**—1. By living, virulent bacteria with potent specific serum.—This method is now used against rinderpest; serum of immunized animals is injected on one side and virulent rinderpest blood on the other. Animals may be immunized against foot-and-mouth disease in the same general way.

2. By attenuated living organisms with serum.—This method, advocated by Sobernheim, is giving good results against anthrax.

3. By dead bacteria with serum.—Proposed by Besredka for plague, cholera, and typhoid; the method is still experimental.

(C) **Passive Immunization.**—The injection of antitoxic and antibacterial serums for prophylactic purposes.

II. Curative Injections.—(A) **Active Immunization.**—By dead microbes and bacterial products (tuberculin and mallein) to hasten reactions leading to healing.—Wright used an anti-staphylococcus vaccine, composed of staphylococci killed by heat, with good effect in the treatment of chronic furunculosis. Other similar vaccines have been used. The method has been suggested also in typhoid fever by Fraenkel and Richardson;[32] here its value is not yet established. Koch's original tuberculin is obtained as follows: Cultures six to eight weeks old of tubercle bacilli upon 4 to 5 per cent. of glycerin-peptone broth are evaporated to one-tenth the original volume and filtered. This fluid contains 40 to 50 per cent. glycerin, and dilutions are made with 0.5 per cent. phenol. Later Koch made use of the organisms themselves. Dried and powdered cultures of virulent bacilli are extracted thoroughly and preserved with 20 per cent. glycerin. This is tuberculin R. Wright[33] has elaborated a promising method of treatment of localized chronic tuberculosis by means of minute doses of tuberculin R, whereby the production of antituberculous substances is stimulated. The dosage and time for the injections are determined by means of the tuberculo-opsonic index. (See Tuberculosis.)

(B) **Passive Immunization.**—1. By antitoxic sera — diphtheria, tetanus, and others.

2. By antibacterial sera—typhoid, cholera, plague, dysentery, etc.

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CHAPTER V.

INFLAMMATION.

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There are so many diverse pictures of inflammation, so many different conceptions of the term, that a definition that will satisfy, while all the more essential, is extremely hard to construct. For the purposes of this article we consider it, following Burdon Sanderson, as the series of local changes which constitute the reaction to injury to, or irritation of, a part. We exclude, that is, from our conception those general disturbances of the system which may be induced by local injury—fever, for example, we hold may accompany, but is not an essential part of, the process: the immediate death of tissues as the result of injury is not included among the phenomena considered, because such death is an arrest of action and not a reaction; though, as we shall point out, the products of tissue death and disintegration, by their effects upon surrounding tissues may secondarily act as irritants and so play a part in the inflammatory process. And making the above proviso, it is seen that the terms injury and irritation become, for our present purposes, synonymous. The very fact that variation is an inherent property of living matter, rendering it capable of continual change, whereby from the simple unicellular organism the complex human organism has been evolved, renders it impossible to draw a sharp line between what is normal and what abnormal, and so renders it impossible to establish a precise definition of any pathologic process. All pathologic processes are but exaggerations in one or other direction—positive or negative—of physiologic processes, and in this particular case it is obvious that there is no sharp dividing-line between a physiologic *stimulus* and a pathologic *irritation*. When we make an ultimate analysis we find that the causes of irritation—and inflammation—are essentially, each one of them, mechanical, chemical, and physical agencies of the same order as those which normally act upon the organism, only now their action has exceeded a certain indefinite limit, whereby similarly the reaction on the part of the tissues exceeds the normal physiologic reaction.

To this definition, as we have urged elsewhere, a further clause must be appended, namely, that inflammation may also be the reaction to *referred* injury. We shall dwell upon this later in dealing with the part played by the nervous system. Here we will only say that the controlling influence of the nervous system upon the organism cannot be neglected, and that, just as the nerve-centers are capable of stimulating the cells to normal activity, so they may stimulate abnormally, setting up abnormal local cell activities, and that in the absence of local injury.

Expressed otherwise, inflammation is the condition or series of conditions into which tissues enter as a reaction to irritation. Any narrower definition throws us into helpless confusion. Thus, certain writers upon surgical pathology, more particularly upon this continent (America), urge that the term be wholly restricted to the local results of *infection;* some would even advance so far as to make it equivalent to suppuration. While we admit, and that freely, the reasonableness of seeking to possess a term which shall separate conditions obviously harmful and demanding surgical interference from those which may be regarded as indicating a healthy reaction, conservative and not demanding interference, the endeavor to delimit our conception of the process in this particular direction must inevitably fail, and this for several reasons. The line that separates the reaction to non-infective from the reaction to infective noxæ is not identical with that dividing healthy from excessive reaction; the reaction to a mechanical injury—a sprained ankle, for instance—may be so severe as to demand the interference of the surgeon, while, on the other hand, a local infection may be of so mild a grade and its progress be so well kept under control by the resisting processes of the organism that surgical interference is wholly inadvisable—as may happen in abortive furuncles. In the second place, inflammation is a condition coming under the purview of all medical men. Not to bring about chaos, it is essential that a term in frequent employment shall possess the same significance in the mouths and thoughts of all members of our profession. The physician dealing from day to day with the results of chronic irritation is so set in his attitude of regarding these as chronic inflammations, and this wholly apart from any sure conviction that they are of infective origin (*e. g.*, chronic interstitial nephritis, hepatic cirrhosis, etc.), that it is not permissible for the surgical branch of the profession to afford a definition which the other great branch cannot accept. Allied intimately with this last is the weight of tradition. During long centuries "rubor," "calor," "tumor," and "dolor" have been at the basis of our conception of inflammatory manifestations, and if with fuller knowledge we have discovered that what is evidently the same process occurs in different tissues with these cardinal symptoms manifesting themselves in different degrees, so that in some tissues one or more may be lacking, nevertheless established usage demands that our definition shall at least embrace those conditions that through centuries have been regarded as inherent in the conception of what constitutes inflammation, and shall not exclude them. It is permissible, that is, to expand our conception of what is to be included as inflammation, but not to contract it in such a way as to shut out conditions which for so long have been regarded as typical. Lastly, it may with propriety be pointed out that the suggested restriction is unnecessary, and this is because we already possess terms which indicate with absolute clearness those very states and processes to which these writers would restrict the use of the term inflammation. In one or other connection "sepsis," "infection," "septic inflammation," and "suppuration" indicate precisely what these writers mean.*

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* We afford these alternatives because the writers in question do not wholly agree among themselves; some recognize that non-pathogenic but saprophytic

Accepting, then, this broader definition, there are certain inevitable consequences. One of the results of the reaction to injury may be repair. We can therefore draw no sharp border-line between inflammation and repair; the two merge, the one into the other. Nay, more, we are forced to see that in some grades of inflammation, and those, too, of an infective nature, processes of a reparative type—such as local cell proliferation—are dominant from the onset.* While there are grades of inflammation in which cell degeneration and destruction assume the upper hand, and while thus inflammation and repair are very far from being synonymous, we have to recognize that the two are closely, not to say inextricably, bound up. However, we shall not discuss in detail the reparative processes in the various tissues which accompany and follow the inflammatory process. These will be considered in a separate chapter.

Admitting this close association, and proceeding, further, to recognize in all cases of inflammation an "attempt at repair," this, it must be pointed out, is far from being equivalent to regarding the reaction of the tissues as purposive. At most it is adaptive. To what an extent the cells of the organism can adapt themselves to altered environment has been impressed upon us of late years by the abundant studies upon immunity, and more particularly by the researches which have followed the enunciation by Ehrlich of his celebrated side-chain theory. There are, however, limits to the capacity for adaptation, and constantly we note that the results, in inflammation, are either far short or far in excess of the needs of this economy as a whole.

Before concluding these introductory remarks it will be well to indicate the scope of this chapter. The amount of material in the literature bearing upon the subject of inflammation is very great, and to treat the subject adequately from all points of view would demand an article much fuller than could here reasonably be presented. Added to which I have already attempted such a treatment of the subject in an article contributed to Professor Allbutt's "System of Medicine," and have very recently revised that article. To repeat, or even to epitomize, what is there written would from every point of view be inadvisable. Here, while upholding the same general conceptions of the process as are there laid down, the object will be to place before the reader a general review of what we regard as inflammation, throughout endeavoring to apply our conception of the nature of the process to the needs of the surgeon. We would at the same

microbes, equally with pathogenic, can produce inflammation; others tend to leave the saprophytes out of the question; others restrict the term purely to the effects of pyogenic microbes, and some again include both the local and the general effects of topical microbic invasion in their conception of the process.

A fuller discussion of these conceptions of inflammation will be found in the first part of my Middleton-Goldsmith lectures, "Medical Record," New York, March 14, 1896.

* Although not, I think, the first observers of this, Gilchrist and Stokes point out that in studying the histologic changes produced by blastomycetic infection, for some little period after inoculation there is not a sign of leukocytic infiltration; all that is observable is local tissue proliferation. Only later as the new cells break down do polynuclear (the term "polynuclear" will be employed as a synonym of "polymorphonuclear") leukocytes appear on the scene.

time suggest that much which is here treated very briefly will be found in that other article in some detail, as will also be found a fairly full bibliography.

THE CAUSES OF INFLAMMATION.

Microbic.—In man, and in connection with acute inflammatory states, microörganisms are the direct exciting cause in the majority of cases. With rare exceptions they form the direct cause of all the serious cases of inflammation in which surgical intervention is demanded in order to arrest the inflammatory process; and in the rare exceptions, such as the conditions brought about by burns and strong corrosive agencies, it is the secondary effects of bacterial invasion that have especially to be guarded against. Had we, therefore, to consider as inflammation only those conditions in which surgical intervention is demanded, then undoubtedly we should be led to regard local infection and inflammation as practically synonymous. As we have pointed out, other conditions must perforce be taken into consideration.

For present purposes three groups of microörganisms may be recognized: (1) the *non-pathogenic*—forms unable to grow and produce toxic material either within the tissues or on the surface, or, again, in the fluids bathing the mucous membranes or discharged from the broken surfaces; (2) the *saprophytic*—forms which are unable to grow within the system, but can multiply in surface discharges or in the fluid bathing the mucous membranes; these may liberate toxic products, and so to this extent be pathogenic through the absorption of their products of growth; and (3) the *parasitic* or *pathogenic* organisms proper—microbes capable of active growth within the tissues under favorable conditions.

For surgical purposes the second of these groups cannot be neglected; the so-called "putrefactive bacteria"—forms found in foul pus and not in the underlying tissues—were those which more particularly led Lister to introduce antisepsis. These saprophytes may find their way into the discharges of open wounds and grow there, and, growing, their products may set up grave irritation, arresting the reparative process. What is more, we have to recognize the existence of the important group of *facultative parasites*. These we include with the parasitic forms proper, but while discussing saprophytism it has to be kept in mind that a large number of pathogenic bacteria, including the forms most frequently encountered, are capable of existing for long periods, and growing on the surface both of the skin and mucous membranes. Pyococci, streptococci, the Bacillus coli, the pneumococcus, the bacillus of blue pus, may be found on the skin, in the mouth, or in the digestive tract of a large percentage of healthy individuals.

With regard to pathogenesis, two main facts have constantly to be borne in mind: First, that the growth of microbes within the tissues is determined not by one but by two factors, namely, the resisting powers of the individual and the virulence or, more exactly, the resisting powers of the microbe. It is the interaction of these two that determines the growth or want of growth of the microbes within the organs, and growth and functional activity must, under ordinary conditions, precede the liberation of toxic substances. The second fact is that bacteria more particularly (we know less regarding other microbic forms) possess remarkable powers of adaptation; their properties vary according to the conditions to which they have been exposed, and among these properties is virulence. Thus it can be shown (Klencki and others[2]) that the Bacillus coli, living a saprophytic and harmless existence within the intestine of one of the lower animals, and there possessing a minimum virulence, may by alteration of the conditions of existence, such as experimental obstruction of the intestine, develop into a highly virulent form, and that in the course of relatively few generations, and may now grow freely in the tissues of the same animal, setting up fatal disturbances.

Bacteria come to the site of their activity either from outside the body at the time of injury, or from some other part of the body; in the latter case the injured area, being a *locus minoris resistentiæ*, is the first part suitable to the bacterial growth, and the bacteria gain access to it not by being attracted thereto by some force resembling chemiotaxis, but rather accidentally, if one may use the term. It is erroneous to think of the blood as absolutely free from bacteria, for if we consider the alimentary tract, we must admit that the absorption of material from the bowel cannot be confined to food materials alone, but that every moment, through the agency of the peripatetic leukocyte, bacteria pass into the blood and lymph streams. Doubtless in health the life of any individual bacterium in the blood-stream is a short one, but there is in this factor a cause of infection and inflammation which is not negligible.

This is still a matter of controversy, and there are many who continue to uphold the view that in health, no bacteria pass beyond the protective layers of the skin and mucous membranes and gain entrance into the body fluids. They hold that the normal organs are germ-free. The latest supporter of this view is de R. Morgan.[3] I can only base myself upon personal investigation and the careful studies made in my laboratory by Ford[4] and Nicholls,[5] and, doing so, must lay down that in health there is a constant carriage of bacteria through the mucous membranes of the pharynx and upper respiratory tract and alimentary canal—particularly the latter—through the agency of the migratory leukocytes, and as constant a destruction of the same by several agencies. The healthy organs are *potentially*, not absolutely sterile.

This is a matter of the highest practical importance to the surgeon. The view here enunciated demands a radical change from the older conception of operative sequels. Sepsis following an antiseptically or aseptically conducted operation is *not* in all cases due to infection at the time of the operation; it may be due to infection from within, the tissues injured by surgical procedures forming a *locus minoris resistentiæ* in which bacteria circulating in the blood and lymph, which otherwise would be destroyed, find conditions favorable for growth. The less the tissues are irritated, the greater their resisting powers and the less the chance of bacterial invasion. This, needless to say, has long been recognized in reference to infection from without; it must be applied to infection also from within. This, further, is the basis of the pre-operative technic or want of technic that is finding favor among our leading surgeons. Do as little as possible to depress the patient, before operation, and thereby keep the resisting powers of the tissues at their highest level. And perhaps more important of all, as a preventive measure guarding against this infection from within, see that the opportunities for such infection are reduced to a minimum, by removing as far as possible the abundant collection of saprophytic and potentially parasitic bacteria present within the intestines, removing at the same time those products of intestinal fermentation which in themselves are toxic, which induce congestion of the intestinal mucosa and, with this, favor increased passage outward of leukocytes into the lumen, and which, being absorbed, tend to lower the resisting powers of the tissues in general. After operation also see that the food is bland and the bowels kept free. This, again, has been empirically recognized as a rational procedure. No one willingly operates without prior purgation, and it is a matter of familiar experience that your chronic invalid kept on simple diet is more likely to have an uninterrupted recovery than your robust, full-blooded man of affairs, upon whom unwillingly you have operated for some minor ailment, without due regulation of the bowels. The value of such purgation lies, we hold, in this diminution of intestinal bacteria and intestinal intoxication. In this connection we may call attention to the recent work of Pirone in peritonitis,[6] and of Archibald, of Montreal, not yet published, upon the formation of peritoneal adhesions. Both these observers have found that, setting up aseptic peritoneal irritation under conditions which precluded the entry of bacteria into the cavity from without, the peritoneal fluid comes to contain the Bacillus coli and other forms, and this when the intestinal mucosa shows no sign of a lesion.

To this "latent infection" must also be attributed many of the "terminal infections" to which Flexner's studies[7] have drawn our attention. Wherever there be a site of lowered vitality beyond a certain grade, the blood which bathes the part may carry a few bacteria (perhaps only a single one), and these are able, in view of the tissue-weakness, to gain a foothold, multiply, produce toxins, cause local irritation, and set up locally a focus of inflammation. Here, in short, we have the explanation of the so-called *cryptogenic* infection.

This is, perhaps, not the place to enter into the fine details of *endotoxins* and *exotoxins*. Suffice it to say that certain bacteria excrete relatively abundant toxins during active function, while others in the main liberate their toxins after their death and during disintegration. The resisting powers of bacteria are not necessarily in the ratio of their toxin production. Here we deal with a matter that is far from being fully elaborated.

This, however, has become more and more obvious, that bacteria set up inflammation not by their mere presence but primarily by the toxins elaborated by them. It is these diffusible toxins that act upon the cells in the neighborhood and cause the changes to be presently discussed.

When these are sufficiently powerful in their action to cause cell degeneration and death, it has to be kept in mind that the products of perverted cell activity and of cell disintegration in their turn act as irritants; there is thus often a combined and cumulative toxic effect. It may be stated as probable that the condition, so closely resembling toxemia, that follows burns of the skin, is a striking example of the disturbances due primarily to cell disintegration.

To discuss the irritative powers of the different bacteria does not belong to our subject, but it may be serviceable to point out that no sharp line of demarcation can be drawn between pyogenic and other pathogenic bacteria. It is true that there are certain species of bacteria which *in man* are specially associated with suppuration; such are notably the pyococcus aureus and albus, the streptococcus, and the Bacillus coli; but these are not of necessity pus-producers in other animals, and even in man they do not inevitably cause abscess formation, and may be found associated with non-suppurative conditions. Conversely, other species of bacteria, which under ordinary conditions of infection do not lead to pus formation in man, may be found to set up abscesses. A notable example of this variation is seen in typhoid fever and in the occasional post-typhoidal abscesses from which pure cultures of the typhoid bacillus may be obtained. Suppuration is not the visible sign of the presence of some particular species of microbe; it is rather the indication of a particular ratio between the virulence of the microbe and the reacting power of the organism.

Traumatic.—This division must include all physical forces which destroy or injure cells of the body, such as wounds, bruises, and fractures of bones. The infliction of surgical wounds, though they be aseptic, falls under this class, and it may be noted that in this class of inflammation the series of events dependent upon irritation is but faintly indicated, because, apart from the knife and the products of disintegration of the killed cells, there is no other irritant; yet even here it must be remembered that the tissues are exposed to a double insult, each one of which is more potent by reason of the presence of the other. The preponderating feature of such an inflammation is the series of events which we mentally connect with repair.

Other causes of this class are friction, movement (as when activity of a part causes a recurrence of an inflammation that has subsided), and electricity.

Thermic.—This class of irritations is closely allied to the last; some cells are killed, others injured, by a greater or less degree of heat or cold; every dead cell is in itself an irritant, the removal of which depends upon its brethren, and every injured cell is rendered in some degree a source of production for more katabolic material than would occur under normal conditions.

Chemical.—The products of bacteria are properly to be classed as chemical; apart from these, the chemical irritants form a small group, including substances or gases which have a destructive action upon the tissues. In this connection, the solutions in common use as antiseptics exert a destructive action on the superficial layers of cells exposed; even weak solutions of corrosive sublimate and carbolic acid, though applied through a short space of time, have the power to kill or injure cells several layers deep. Certain toxins produced in the animal or plant body, such as the venoms of insects and reptiles, cantharides, mustard, and croton oil, are capable of setting up inflammatory changes in tissues.

Nervous.—If, as already stated, we have to admit that the cells of a part are capable of *stimulation* through the nerves, we must accept also that still more intense nerve action may set up cell *irritation*, resulting in undue reaction on the part of the cells. We confess to an unwillingness to admit that the results of such irritation are to be regarded as a true inflammation, nevertheless, save in the one particular that it is accompanied by little escape of leukocytes out of the vessels into the affected part, such localized nervous irritation may be indistinguishable from acute inflammation due to direct injury, and it is impossible to lay down that leukocytic migration is the essential sign of the inflammatory process.

What is perhaps the best example of such neurotic inflammation is best seen in herpes zoster, a condition which the researches of Head and Campbell[8] show definitely to be a sequel to a peculiar regional disturbance of the posterior root-ganglia. Similarly an acute redness, swelling, heat and pain, strictly localized and sometimes leading to such extensive exudation of fluid from the vessels that vesication is produced, may follow hypnotic suggestion of injury inflicted. In such cases there is a characteristic tendency for the corresponding region of the opposite side of the body to be likewise involved.

Of greater surgical interest is what may be termed *sympathetic inflammation;* that is, the reaction exhibited in other areas secondary to active inflammation in a particular region. Abscess involving the root of a tooth may thus be accompanied not merely by pain referred to regions innervated by other branches of the fifth nerve and by facial neuralgia, but by actual swelling and redness of the same side of the face. So also a relatively slight injury to the knee-joint may be accompanied by great swelling and indications of irritation of the tissues surrounding the joint.

In these and like cases it is clearly not the direct noxæ that cause the inflammatory manifestations. We have to deal with a "referred injury" and subsequently reaction. The irritation of a sensory nerve of the primarily inflamed area influences the whole of the neurone of which it is a part, rouses that to such activity that stimuli irradiate from it to all the associated neurones. Stimuli passing from these to the higher centers convey to the brain the impression that the parts innervated by them are also injured—"referred pain." Similarly reflex action brings about vascular and tissue changes not only in the area of primary injury, but also in the areas of distribution of the associated neurones. It has to be remembered, therefore, that the extent of territory involved in the inflammatory process is not always a sure indication of the extent of active injury. The personal equation of the patient has to be taken into account, *i. e.*, the excitability of the nervous system of the individual.

These considerations throw not a little light upon what we may term sympathetic treatment. The converse, that is, must also be true, that by treatment directed more particularly to areas innervated from the same zone or level in the spinal cord, we can influence the neurones passing directly to the area of injury, and, doing this, are enabled to modify the symptoms and process so far as these are controlled by the nervous system. We gain thus a rational basis for counter-irritation.

DEGREES OF IRRITATION, AND THE RESPONSE THERETO.

We have already incidentally touched upon the factors leading to variation in the response to injury. Here we hold it important to discuss them somewhat more fully.

No two cases of inflammation behave exactly in the same way, because each individual problem has varying factors, as follows: (1) Irritant agents vary in their ability to injure. (2) Tissues vary in resistance, and so differ in the speed and thoroughness with which they carry on the various steps of the process of inflammation.

The former of these statements, that irritant agents vary in their ability to injure, needs no explanation as long as we are considering trauma or thermic and chemical irritations. It is a fact long ago proved that bacteria, similar in morphologic and cultural characters, differ widely from one another in virulence; not only is this true, but the same bacterium seems to differ in this respect from time to time, though this may be due not only to change in its inherent qualities, but also to the changing powers of the tissues in the production of antitoxins, bacteriolysins, and other materials antagonistic to the bacterium's life and activity. The resistance of tissues is probably yet a more variable factor, and it is especially this quantity (which to medical science is entirely incapable of exact determination, and which must ever remain so) that lends an ever new aspect to the study of each case of inflammatory reaction. If we were able to gage in some way the resisting power of a human body, there is no probability that this quality would be found to remain unchanged for a single hour.

The tissue of every organ in the body may be divided into two classes of material—the parenchyma and the supporting tissues. Perhaps one ought to make an exception in the case of those structures that are by their very nature supportive, such as bone, cartilage, or tendon; but if this be granted, it still remains a fair generalization. Parenchyma is specialized tissue, which has a special function, which is highly trained, and set apart—a kind of "professional" class; the supportive tissues, on the other hand, less specialized, do a less high class of work, and may be likened to the "laboring" class. One may even go further, for purposes of illustration, and point out that the parenchyma does not reproduce readily, is not easily replaced, is damaged by comparatively slight stimuli, and, if destroyed, its function can be taken up only by cells similar to it—for example, a nerve-cell body, a liver-cell, or a muscle fiber. The supportive tissues, on the other hand, uneducated to special work, are prone to reproduction, are untouched by slight stimuli, and their work can be done by tissues that merely approximate to them, without being their exact counterparts; such is connective tissue in general. These two kinds of tissue lie everywhere side by side and are exposed to similar irritations, to similar toxins, are bathed alike in toxic body juices, yet they react in different degrees, and a toxin severe in its effects upon the "professional" or high-class parenchyma cell may trouble but little his "laboring-class" brother, the connective-tissue cell. This important point may be illustrated by returning to the simile of the commonwealth: the questions of daily politics constantly agitate the minds of the higher classes of citizens, but the laboring classes are moved from their daily routine only by something that shakes the very foundations of the nation.

Reverting to the differing degrees of irritation, we may draw up a working scale of, for example, toxins. Certain of these, which we will for the moment designate degree A, are so strong that they kill at once a certain cell with which they come in contact; others, degree B, are not strong enough to kill instantly, but they so injure the cell that it enters at once into the stages we call cloudy swelling, granular degeneration, or whatever name we employ, and finally dies; this process we call bio-necrosis. Yet others, degree C, injure the cell so that it enters this condition of successive ill-being, but finally recovers; this is not exactly bio-necrosis, but, if we dare coin a word for present use in this chapter, it might be said that the toxin is bio-necrescent, that is, tending to bio-necrosis. Finally, other toxins, yet weaker, degree D, irritate the cell within the limit of its reactive powers, but without exhausting the same, and its irritation is shown by reproduction, by phagocytosis or chemiotaxis, or any other function we can attribute to the cell that is "roused." And this is true not only in regard to different toxins, but in regard to different degrees of concentration of the same toxin. We have to recognize, in short, the law that the agent which in high dilution or small quantity acts as a stimulant to the cell, becomes in greater concentration a poison to the same.

It will be at once evident that, in the kidney, for example, toxic blood may severely injure a tubule cell (degree B), yet may not be able to do more than rouse the connective tissue to reproduction (degree D). Every cell of the body that comes within the "sphere of influence" of a toxin reacts in some degree thereto, degree A, B, C, or D, and this applies not only to fixed cells, but to every lymphocyte, leukocyte, or wandering tissue cell whose business calls it into the area of irritation at the time; the result of any inflammation depends, therefore, on the sum total of these million tiny problems, and the total determines whether the balance is in favor of or antagonistic to the body.

THE INFLAMMATORY PROCESS.

That we may gain a clear picture of the process of inflammation in ordinary, let us select what we may regard as a typical case and follow the successive stages. Having done this, we can the better proceed to analyze the various factors involved in the production of the effects noted and consider the variations in the manifestations of the process according to the region involved and the intensity of the irritant.

As bacteria are the most frequent cause of serious inflammations, and suppuration is the outcome which most often demands treatment, and as, further, the softer tissues are most frequently the seat of inflammatory changes, it will be most serviceable to take as type the series of events leading up to abscess formation in subcutaneous tissue. This can readily be followed by inoculating a few drops of a culture of a definitely virulent pyococcus aureus into the subcutaneous tissues of a series of rabbits, killing them at successive periods, and, after due preparation, examining sections of the tissues from the site of inoculation.

Doing this, we observe that, in the first place, there is little immediate reaction; the vessels do not immediately become congested; it is some four hours before definite changes are recognizable in the part, and then what is most noticeable is that the vessels have become prominent and are filled with abundant white corpuscles, whereas in normal tissues the veins and capillaries are on section little noticeable and contain relatively few leukocytes. Here, however, these white corpuscles already show *margination, i. e.*, they are in places arranged in intimate contact with the vessel walls (Fig. 36). In the tissue around the needle track and outside the vessels there are already more leukocytes than usual, both polynuclear * and mononuclear, the latter (contrary to what is found later) preponderating. It is also to be noted that the connective-tissue cells of the part have become swollen and more prominent. As for the inoculated cocci, the majority are free, but already a fair number are to be seen within certain of the leukocytes, as, indeed, within some of the swollen connective-tissue cells.

In ten hours—we follow Hohnfeldt[9]—the conditions are more pronounced; the vessels even are more congested; margination becomes more general, and, what is more, the various stages of passage of the leukocytes (polynuclear) through the walls of the finer vessels can be observed here and there, and coincidently there are now abundant leukocytes, mainly polynuclear, immediately around the vessel in the perivascular spaces, and spreading from them into the surrounding tissue, where, also, judging from the number of cocci, those injected are undergoing active proliferation. Already the polynuclear leukocytes are massed mainly around the microbes; mononuclear leukocytes are present in the peripheral zone.

Within twenty hours the accumulation of leukocytes and proliferation of the cocci are still more marked. The fibrils of the original tissue of the part are widely separated by masses of the cells; they are, indeed, difficult to follow on account of the overlying leukocytes.

Only in forty-eight hours—in the rabbit—is an abscess properly developed, a well-defined mass of cells distinct from the surrounding tissue. Such a mass shows a surrounding zone of congestion and infiltration, in the capillaries of which margination and passage out of leukocytes is still a prominent feature, *i. e.*, more cells are still making their way into the part. Within this zone is a densely packed mass of polynuclear leukocytes intermingled with abundant cocci. Large numbers of the leukocytes contain cocci, but in the center of the mass the cells show clearly degenerative and disintegrative changes, their nuclei exhibiting fragmentation. Within the abscess proper there are now no traces of tissue structure; the swollen capillaries have wholly disappeared, as though having been dissolved; so also the connective-tissue cells and fibrils have vanished, and their place is taken by the living and dead leukocytes—pus cells; the tissue is replaced by pus.

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* The term polynuclear is used as a synonym of polymorphonuclear throughout this chapter.

It is deserving of note that in this earlier period of abscess formation, while the proliferating cocci are mainly within the abscess and most abundant toward the center, some are to be seen in and even beyond the boundary zone, either free or taken up by leukocytes or by endothelial cells of the capillaries.

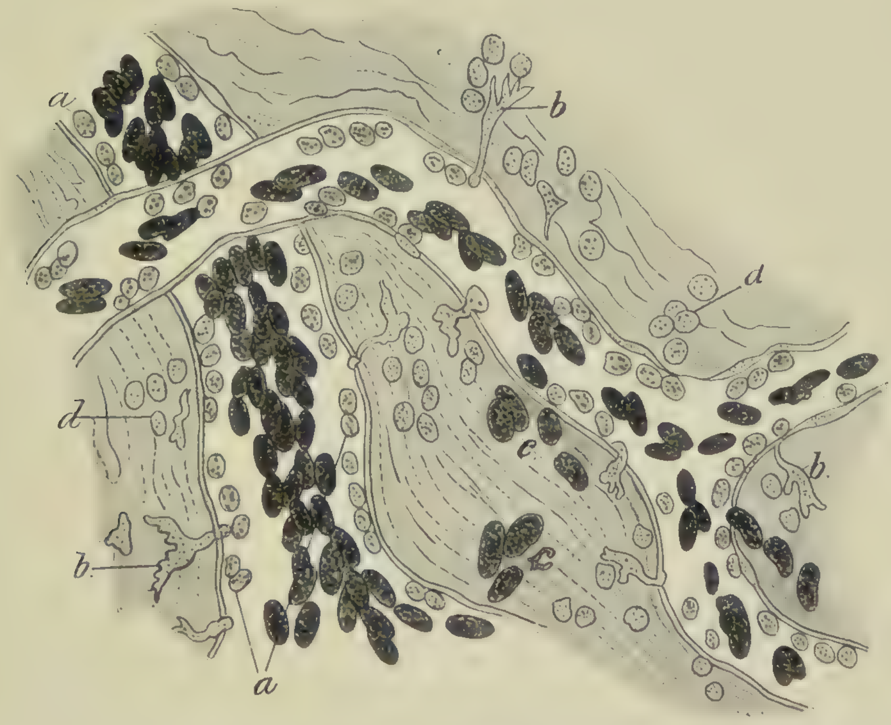


FIG. 36.—INFLAMED MESENTERY OF FROG.

To show margination of leukocytes in the dilated capillaries (*a*); migration of leukocytes (*b*); escape of red corpuscles (*c*); accumulation of leukocytes outside the capillaries (*d*) (Ribbert).

One of two processes may now occur—either the further spread of the process or resolution. We shall not discuss the former to any extent, for it will be dealt with in the chapter devoted to the subject of abscesses. Suffice it to say that the accumulation of leukocytes continues; the area of infiltrated and destroyed tissue becomes larger and larger; around it is still to be seen an "inflammatory area," an area of congestion with margination and migration of leukocytes; and still in this area cocci are to be seen, which from their numbers are undergoing proliferation. And these cocci may not merely remain here, but, being carried into the efferent lymph-stream, or even by leukocytes into the blood-vessels, may further be carried to a distance and there originate other foci of inflammation and metastatic abscesses. In these spreading abscesses the marginal zone is far from distinct; there is nothing of the nature of what used to be termed a pyogenic membrane; instead of any sharp boundary there is a diffuse infiltration of the surrounding tissue with degeneration and necrosis of the same.

The other process—that of resolution—is characterized by the fact that when the abscess has reached a certain size it is noted that the cocci are absent from the outer zone of leukocytic infiltration. Either the cocci are so weak or the leukocytes so strong and so numerous that if the microbes be conveyed into this zone they are destroyed. Clearly, this absence indicates that the organism has drawn up sufficient forces to neutralize the destructive powers of the microörganisms. When the point is attained, although sections still show the existence of cocci within the purulent center of the abscess, and that leukocytes are still passing from the surrounding congested capillaries into the part, it is to be observed that coincidentally there are signs of other activities in the surrounding zone.

In the first place, there are evidences of absorption and the abscess becomes relatively smaller in size. This absorption is due, (1) to the liquefaction of the dead leukocytes within the abscess and the diffusion of the fluid, and (2) to actual return of leukocytes from the part into the blood-vessels, lymph-spaces, and so into the lymph-vessels passing from the part. Where the abscess is of any considerable size we observe further a sharp distinction between the surrounding congested zone and the central mass of pus cells; the passage of leukocytes to and from the vessels is still occurring, but is not nearly so extensive, and the inflammatory or pyogenic zone becomes clearer because less cellular. Next, in such an abscess in the same zone two other processes can be made out, viz., the production of new vessels toward the central collection of pus and the definite indications of new tissue growth around these vessels in the form of larger rounded, oval, or spindle-shaped cells, these latter being definite fibroblasts—the precursors of the connective-tissue cells; and these in their turn control the formation of wavy bundles of connective-tissue fibrils. Through all these processes, first, the pus gradually disappears; and, in the second place, the area it occupied shrinks and is filled with new vessels and surrounding new connective tissue—with, in fact, what is termed granulation tissue. As this grows older it cicatrizes and becomes dense and very fibroid, at the same time undergoing much shrinkage. These latter changes will be discussed in fuller detail in the chapter upon irritative processes.

Recalling the data afforded in this sketch of the course of an acute inflammation, it is seen that the process is one which affects all the components of the part—blood-vessels as well as the specific tissues, fixed cells as well as free and transient. We would now proceed to analyze and discuss in a little more detail the part played by the various factors.

I. Circulatory Changes.—When an irritative substance acts on the tissues there occurs a momentary contraction of the arteries with consequent relative anemia, and this is soon followed by a more lasting dilatation. These changes would seem to be very largely the direct effect of the irritant upon the vessels, for they occur in limbs cut off from relationship with the central nerve system by section of the nerve-supply.

With the dilatation of the vessels the part becomes hyperemic, the capillaries and veins distended and prominent. But here is the remarkable feature: *à priori*, we would be inclined to imagine that with widening of the channels there should be a more rapid blood-flow through the inflamed area, a condition of active hyperemia. Such a condition of increased blood-flow we can produce by sundry stimuli, for example, by the action of warmth applied to the part. The part becomes reddened—a bright arterial red; and, what is more, we can, by these means, so promote the flow of blood through a localized area and so lessen the peripheral resistance that the arterial pulse is carried through to the efferent veins, and the blood in these is of arterial and not venous color. Such active hyperemia does show itself momentarily in an ordinary inflammation; there is first seen the livid flow of blood from the dilated vessels; then in a short period this gives way to a distinct slowing of the stream; this slowing in acute cases and in some vessels may even go on to complete arrest and stasis. This, however, is exceptional. The dilatation of the vessels is characteristically, then, accompanied by a slowing of the blood-stream, such a slowing as we encounter when there is obstruction to the veins leading from a part—in conditions which we term *passive* hyperemia or passive congestion. And this occurs without evidence of the existence of any such peripheral obstruction. Whence we conclude that as, despite the dilatation of the capillaries and veins of the area, which in itself should favor a freer flow, the onward progress of the blood is delayed, there must be some increased local resistance to onflow, some change either in the constitution of the blood itself or in the lining of the vessel walls leading to increased friction.

That some change occurs in the blood itself is evident. There is increased passage of the plasma or fluid of the blood into the surrounding tissues. Not only do we have the gross evidence of this in the swelling and somewhat edematous condition of the part, and, where a wound has been made, in the free pouring of serum from the surface of the wound, but experimentally it can be shown that the discharge of lymph from the inflamed area is greatly increased.

Samuel's[10] figures obtained from the dog's foot are very striking: the untreated foot in three hours gave 4 c.c. of lymph having 4 to 5 per cent. of solids; the foot subjected to venous obstruction gave 28.5 c.c. of lymph containing 2 to 3 per cent. of solids; the inflamed foot in the same space of time gave 28.5 c.c. of lymph containing 7 per cent. of solids. It was, in fact, so rich in proteid matter that it time and again coagulated in the canula, so that the figure 28.5 c.c. does not represent all the lymph which could have passed along the vessels.

But if the mere act of dilatation of the thin-walled vessels led to increased transudation of fluid, and if this were the only factor, there should be no such condition as active hyperemia; everything leading to vascular dilatation should be accompanied by slowing of the flow. This we know is not the case. It is obvious that relative concentration of the blood cannot be the only factor involved. We have to conclude that the endothelium lining the vessels is affected, and this in such a way as to interpose an increased friction. As a matter of fact, and as we shall point out later, the vascular endothelium in the inflamed area is markedly affected. Years ago Lister pointed out that if an indifferent fluid containing suspended particles, such as milk, be passed through an inflamed area it undergoes a similar arrest, its suspended particles accumulating within the vessel. Some change, then, occurs in the physical characters of the endothelial surface. Borrowing from bacteriologic terminology, we might say that the surface becomes more *agglutinative.*

This subject of inflammatory hyperemia looms large at the present moment, thanks to the remarkable clinical studies of Bier, of Bonn.[11] The time is perhaps not yet ripe to appraise the value of Bier's various methods; a wider testing of results obtainable is requisite. This, however, may be said, that it has been abundantly shown that in certain conditions of acute localized inflammation recovery is materially hastened by promoting the passive hyperemia which characterizes a normal inflammation. Here it may be asked: What are the results gained from this hyperemia? So far as we can at present see they are the following:

1. *Increased Transudation (Exudation) of Fluid from the Vessels into the Tissues.*—The mere effect of increased intravascular pressure with the associated thinning of the walls of the dilated vessels must bring this about. Thereby there is produced (*a*) a dilution and (*b*) a flushing out of soluble irritants. It will be noted that this flushing is but an exaggeration of the normal function of the lymph, which is constantly carrying off katabolic material from the cells. Possible modification in the properties of the transudate we will discuss later. (*c*) Increased nutrition of the tissues of the parts. This Virchow regarded as a main factor in the inflammatory process. It is, however, doubtful whether in an acute inflammation the nutritive function of the exudate is very prominent. It may be pointed out that the most active exudation occurs early in the process when tissue proliferation is little or not at all evident, and that when the irritant is most virulent, and the cell destruction greatest, the exudation is most pronounced. The relative paucity in oxygen of the blood in the congested vessels withdraws from the exudate one of the main tissue foodstuffs, and judging from the appearance of the tissue cells disintegrative changes outclass assimilative at this earlier period. But at the margin of an inflammatory area where the hyperemia is still pronounced and the toxic substances are not concentrated, the active cell growth suggests undoubtedly increased assimilation on the part of the cells.

II. *Increased Migration of Leukocytes.*—It is needless to repeat that this increased migration is a pronounced feature of inflammatory hyperemia. Here we may note that active hyperemia with rapid passage of blood through the vessels is unaccompanied by such migration: the leukocytes are hurried along in the axis of the stream. How these leukocytes act we shall discuss in a succeeding section.

(*d*) There are indications that, apart from alterations in its composition brought about by the dissolution of migrated leukocytes, and apart also from the soluble toxins it comes to contain which are liberated from active and dead bacteria, the exudate differs in its composition from the normal lymph. Thus aqueous humor has under ordinary conditions singularly low bactericidal and other powers: even in animals that have been immunized against one or other disease its properties are insignificant. This has been known for long. Immunize a rabbit against ox blood, and the aqueous humor possesses no hemolytic properties; or against typhoid, and its agglutinating powers are very low. But, as Wessely[12] points out, irritate the eyes of such rabbits by making subconjunctival injections of 5 or 10 per cent. salt solution, and in the first case the aqueous humor becomes strongly hemolytic; in the second, actively agglutinative. The local inflammation has affected the ciliary vessels and the fluid thus becomes modified. This example is, however, not wholly beyond criticism. Wessely has not proved positively that there is not an associated passage out of leukocytes, which, breaking down, have endowed the humor with these properties.

III. *Relief of Pain.*—This is particularly emphasized by Ritter[13] and Bier. Every form of hyperemia lessens the sensation of pain. The serous infiltration of the tissues lessens the sensibility of the nerves, just as Schleich has shown for all possible edema-producing media. If the passive hyperemia be suddenly increased, as by moderate compression of the veins above an inflamed area, there is a temporary increase in pain, but this soon gives place to a feeling of comfort and well-being in the part.

Judging from the effects when it is purposely increased, as by Bier's method, this inflammatory hyperemia is in the main distinctly beneficial. With Bier we would not ascribe the benefit to any one factor: the dilution of the irritant may well play a part; the flushing out and removal of the irritant also, as, again, must the increased migration of leukocytes and the accumulation in the area of increased amounts of antibacterial and antitoxic substances. As one who has evidently not studied at first hand leukocytic activity, Bier is inclined to rate as of small account the part played by the leukocytes in conveying these protective substances to the part. For myself, I am inclined to rate it very highly and to see in the increased blood-supply and slowing of the blood-flow processes which peculiarly favor increased passage of leukocytes out of the vessels. To this beneficial activity of the leukocytes I shall return. At the same time it must be borne in mind that, as already stated, pathologic processes being but exaggerations of normal ones, the very fact that they are exaggerated is apt to make them unbalanced. The very fact that the development of additional hyperemia promotes often the more rapid healing of acute inflammation, indicates that the natural reaction is often inadequate. In other cases, on the contrary, the hyperemia and attendant increased passage of lymph out of the parts flushes also the organic irritants, such as pathogenic bacteria, out of the area of local growth.

It is true that one swallow does not make the summer, and that a solitary pathogenic microbe so flushed out stands a chance of being destroyed in the more healthy tissues to which it is carried; but if at any point in the path such flushed-out bacteria accumulate in any quantities, they may through their toxins overcome the tissue resistance and, growing, set up a focus of metastatic inflammation.

The Exudate and Fibrin Formation.—The inflammatory exudate differs from ordinary transudates (lymph and serous fluids) in its higher specific gravity and its definitely increased amount of proteid matter. It in general coagulates easily and is apt to contain abundant leukocytes. The studies upon its properties are as yet far from complete, but it may be said that, as a general rule, it is richer than is ordinary lymph in the products of cell degeneration and dissolution, notably in bodies of the nature of enzymes and proteolytic, antitoxic, and bactericidal substances, added to which in bacterial inflammations it becomes more toxic, containing diffuse bacterial toxins.

In discussing hyperemia I have already pointed out some of the main properties which may be ascribed in this increased inflammatory exudate. Here I would more particularly discuss the formation of fibrin in such. That formation may and does occur within the tissues, and, by proper reagents, such as Weigert's stain, may be often demonstrated in the inflammatory area, though often, again, it is absent. Pyogenic organisms, for example, have marked proteolytic powers, and their presence leads to its dissolution or non-appearance. In some conditions we find it characteristically within the lymph channels, the lymph undergoing coagulation.

It is, however, in connection with inflammation of serous surfaces and in the so-called inflammations of mucous surfaces that fibrin characteristically tends to form, and its formation in these regions is associated with the breaking-down of leukocytes. It is to this fibrin that we owe the plastic adhesions in serous cavities, and these adhesions play a most important part in limiting the spread and generalization of many bacterial inflammations. They do this in part by immobilizing the immediate surrounding viscera; in part also the fine and abundant meshwork of delicate threads acts as a definite hindrance to the diffusion of the bacteria. The fibrinous network is, indeed, of the nature of a filter, admitting the diffusion of fluid to a certain extent, but hindering the passage of solid particles.

The beneficial effects of this fibrin formation are often very remarkable. One has but to study the highly vascular and sensitive great omentum in connection with localized abdominal inflammation to observe how time and again a portion of it becomes firmly cemented over some infected area of one or other abdominal organ. We have found such omental adhesions over danger-spots on the walls of the stomach and abscesses about to burst in the liver, over ulcerated areas of the duodenum and on the very floor of the pelvis, covering over the stump of a removed uterus. The constancy with which these adhesions occur in connection with the inflamed appendix I need scarcely mention.

But here, again, as has been pointed out,[14] we must simultaneously recognize that it is not purposive, that time and again these adhesions are productive of harm. The abundant covering of fibrin over the pleura may often greatly prolong a pleurisy by delaying absorption, and in the peritoneal cavity there may be a kinking and obstruction of the bowels even before organization has commenced; while with organization and replacement of the fibrin by bands of connective tissue (for the formation of which the fibrin acts as a framework) similar obstruction, torsion, internal hernia, and so on may be brought about. To repeat once again, the various phenomena of inflammation while tending to repair are not purposive—they are at most adaptations and cannot and do not accurately fulfil all the needs of the economy.

The Vascular Endothelium.—As already indicated, it is due to some change in the endothelium lining the capillaries and veins that the leukocytes are arrested at the site of inflammation, and that the blood-flow becomes slowed, the adhesion of the cells to the vessel walls being due, it would seem, rather to change in the endothelium than to change in the leukocyte itself. Of what that change is, we are ignorant; we only know this, that these endothelial cells are not, as we were taught to regard them in the past, passive "tiles" lining the vessel, but are capable of performing various functions. They can contract and dilate; they govern to some extent the quality of the fluid passing through them in the different tissues according to the functions of those tissues; they have been seen to send out pseudopodial processes (Werigo [15]), thereby seizing upon bacteria in the blood-stream which have come into contact with them; and, along with many other observers, we have seen such bacteria actually within their substance, there undergoing digestion (phagocytosis).

The idea that used to be taught, that there is a cement substance between the cells—that the tiles are laid in cement—is nowadays given up, or at least greatly modified. As Kolossow [16] and others have shown, adjacent endothelial cells are joined directly the one to another by delicate protoplasmic bridges between which are minute spaces. When the capillary is contracted these are invisible and practically non-existent. When, on the other hand, it is dilated, these spaces are actual, and not merely favor the increased passage out of fluid from the vessel, but form the regions of least resistance through which (rather than through "stomata" or through the substance of the endothelial cell itself) we are led to believe that the leukocytes project a pseudopodium and eventually insinuate the whole body. In intense hyperemia and inflammation of capillaries that have little support, the widening of these spaces may become such that the red corpuscles are forced through them, and, as in acute lobar pneumonia, we may have hemorrhage by diapedesis. In less acute inflammations, or where there is a stronger supporting framework, permitting no such extreme dilatation, the red corpuscles, we are inclined to think, pass out only through the larger lacunæ made by the previous passage of a leukocyte. In inflammations of a still less severe order, leukocytes alone may migrate without any of the passive erythrocytes becoming pushed through the wall.

Yet another and still debated function of the vascular endothelium is that of growth and cell multiplication—debated so far as the growth is capable of affording origin to one order of wandering cells—to certain intravascular mononuclear hyaline leukocytes. In the inflamed area it is a matter of familiar observation that the cells of the vascular endothelium are more prominent than usual, their nuclei larger, their cell bodies bulging to some extent into the lumen of the capillary. And when bacteria are injected into the circulation after some hours they may be found in the capillaries of the lungs and other organs, surrounded by not only the ordinary polynuclear leukocytes, but also by other cells of a so-called epithelioid type, large and clear. The evidence is accumulating that cells of this type are of endothelial origin.

Closely allied to this debatable matter is the question of the origin of cells of like nature outside the vessels and in the tissues proper from the endothelium of the lymphatics. Whereas only a few years ago the trend of opinion was that all wandering cells in the tissues were of hemic origin, derived from the leukocytes of the blood, once again the view is gaining ground that not a few of the mononuclear cells seen in an area of inflammation are the direct derivatives of preëxisting cells of the part.

It may well be that the modern pathologist is guilty of ultra-refinement in seeking to distinguish between the exact seats of origin of the cells in question, whether from the lymphatic endothelium, the connective-tissue cells, or the vascular endothelium. Although this is debated by some, the vascular endothelium is, from embryologic and physiologic considerations, to be regarded as modified connective tissue. Studying the development of new vessels in granulation tissue, although toward the side of the vessel the new endothelial cells and the new capillaries arise from preëxisting endothelium, nevertheless toward the side of the surrounding tissue these new cells are seen to send out processes joining with, and indistinguishable from, those of the surrounding connective-tissue cells. Nor are these processes characteristic of the young capillary only—the finest capillaries of the developed animal exhibit them, as was shown years ago by Stricker in the case of the frog.

And, on the other hand, as regards the lymph spaces: All connective tissue is practically a series of lymph spaces, and the cells we picture as bounding these spaces are the identical cells which at other times we picture as the connective-tissue cells of the stroma. The lymph meandering through these spaces finds its way almost imperceptibly into larger channels, the lymph channels, which now are lined with a more specialized endothelium, which endothelium is as intimately connected as was the vascular with the surrounding connective-tissue cells. When any of these slightly differentiated cells reproduce, they swell to many times their resting size and give rise to a large, clear, acidophilic cell intensely phagocytic, more particularly for other cells and for cell débris, though bacteria are also taken up by them. These cells are of the same order as the larger cells given off from the endothelium of serous surfaces in inflammation, first studied by Cornil and Ranvier. According to the nature of the stimulus, the blood-capillary thus would seem capable of giving off new cells either into the lumen or externally.

The Blood-cells.—Coincident with the dilatation of the vessels and the slowing of the blood-stream the leukocytes are seen to gather in increasing numbers on the inner surface of the capillaries and veins, to undergo margination, and to make their way through the walls. The process is an active one, by the projection of a process or pseudopodium through one of the intercellular spaces, and gradual streaming of the semifluid protoplasm of the cell through the minute orifice until the whole leukocyte comes to be on the other side. There is satisfactory evidence that the process is due to *chemiotaxis*, or attraction of the cell toward areas in which certain substances are in greater concentration. If, for example, there be inserted into a vessel a minute tube containing the products of growth of certain bacteria dissolved in a bland fluid, such as physiologic salt solution, the leukocytes are found to wander actively into the tube from the blood-stream, while with other substances—dilute acids, for example—not a single leukocyte wanders in; they are, if anything, repelled. Similarly, if pyogenic bacteria, or their products, be injected locally into a tissue, the leukocytes migrate to the region of inoculation. If at the same time the same products be injected into the circulating blood, there is no such migration. The difference in concentration of the chemiotactic substance in the blood and lymph respectively is not sufficient to attract the leukocytes from the one region to the other.

This view demands that we regard the irritant substances which insure a purulent or leukocytic inflammation as of a diffusible nature, and, further, that we accept the view that when the blood circulates through a vessel not only are there currents of fluid passing from the vessel into the surrounding tissue, but also that there occur currents in a reverse direction from the tissue into the vessels, whereby their diffusible substances come to act on the leukocytes. We need scarce remark that the observations of the physiologists on absorption and the studies upon osmosis through membranes wholly support this contention.

The extent of this attraction and the consequent extent of leukocytic infiltration of the tissues depend upon several factors—more particularly upon the nature of the irritant and the concentration of the same. Very acute inflammation may be associated with little or no leukocytic migration—the leukocytes are repelled. Less acute inflammation set up by the same species of microbe, but of lessened virulence, may present abundant migration. It is a matter of common observation that as between a typhoidal peritonitis and one associated with the B. coli, in the former few leukocytes are discharged from the vessels—what pus there is, is thin and the tendency to the formation of fibrin is slight,—whereas in the latter the pus is thick, abounding in leukocytes and easily forming adhesions.

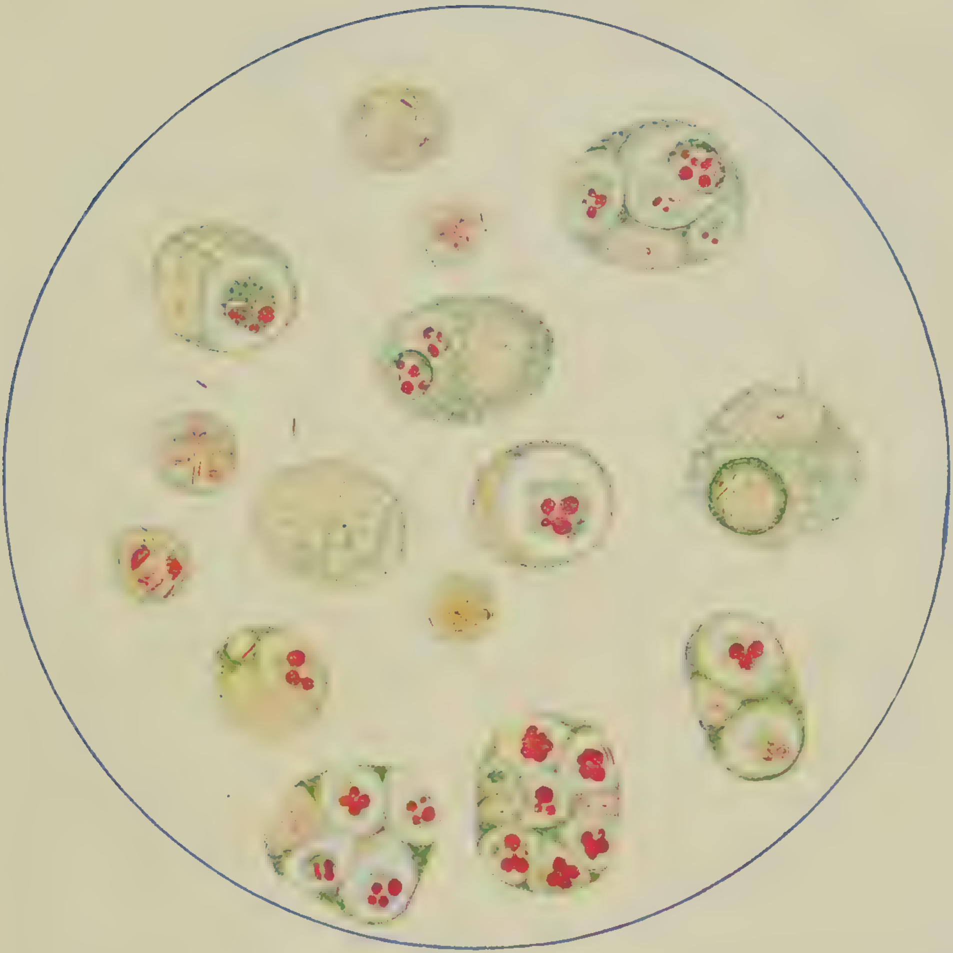
As already indicated, the red corpuscles are passive agents in the inflammatory process; their presence outside the vessel walls may be regarded as largely accidental. The white corpuscles, on the other hand, play an active part, and here a few words must be said regarding their origin. At one time all were regarded as derived from the blood, and still we regard the terms white corpuscle, leukocyte, and wandering cell as synonymous, though we make the distinction between the hematogenous and histogenous leukocytes—those passing to the part from the vessels, and those not so passing, but derived from multiplication of one or other element of the tissues. It is with the former that we are at present concerned. Those seen in normal blood which undergo migration are (1) first and foremost, the polynuclear, (2) the lymphocyte, and (3) the eosinophile.

1. **Polynuclear Leukocytes.**—These are the common pus cells and are the form which migrate in predominant numbers in cases of acute inflammation. As the name implies, they are characterized by the varying and irregular shapes of their nuclei, which are lobate, the processes joining the little lobes being frequently so fine that the individual cells appear to be multinuclear (Plate III). They are actively phagocytic, especially for bacteria; the indications are that both in activity and in the process of dissolution they liberate antitoxic and bactericidal substances. Leber, indeed, has shown that aseptic pus free from microbes contains proteolytic and other substances, while Denys, Buchner, and other observers have demonstrated that these cells, accumulated by setting up a nonmicrobic inflammation in the pleural and other cavities and separated from the serum in which they are suspended, are very much more bactericidal than is that serum, or than the other fluids of the body. They may wander back to the circulation by way of the lymph or the blood-stream, or may die and undergo disintegration at the site of irritation, or may be ingested by the tissue and other cells of the inflammatory area. All the evidence is against these cells taking part in new tissue formation. They are the main phagocytic agents and the main producers of substances necessary for antitoxic and bactericidal processes.

2. **Lymphocytes.**—We are not concerned with the interesting problem of the relationship between the lymphocytes and the larger mononuclear cells of the blood. We find true lymphocytes in the circulating blood, we find them also in areas of inflammation, and more than one observer has seen them in the actual process of migration through the vessel wall. They are characterized by possessing a relatively large, deeply staining nucleus and a relatively small amount of surrounding cytoplasm. They are but slightly amœboid. In some chronic and subacute inflammations they are found in preponderating numbers, often in close relationship externally to the blood-vessel. There are indications that under these conditions they have been derived in part by migration, in part by proliferation of the lymphoid tissue normally present in the perivascular sheath. They are not phagocytic for bacteria, but can ingest solid particles. It must be admitted that these cells may give rise to large lymphocytes with relatively more cytoplasm and less strongly staining nuclei, and to the so-called plasma cell. There is no evidence that these plasma cells return to the blood-stream or are actively amœboid; they are especially likely to occur in chronic inflammation, and probably take a part in the formation of new fibrous tissue.

As regards the large mononuclear cell found in the blood, we can only say that exactly similar cells are found in the tissues in inflammation.

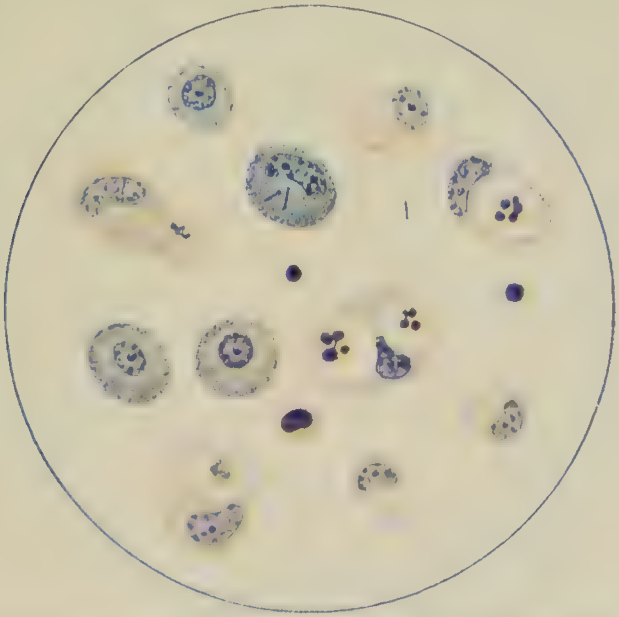
PLATE III.



Peritoneal Fluid Forty-eight Hours after Intraperitoneal Injection of Bacillus Coli Communis.

Showing vacuolation of protoplasm, digestion of polynuclear leukocytes, and the digestive vacuole (Beattie).

(From the "Journal of Pathology and Bacteriology").



Peritoneal Fluid Thirty-six Hours after Intraperitoneal Injection of Bacillus Coli Communis.

Showing actively phagocytic mononuclear cells, and similar less active, darkly stained cells (Beattie).

(From the "Journal of Pathology and Bacteriology").

It is thus quite likely that these are of tissue origin. It may be that both arise from a common source, namely, the capillary endothelium; if this be so, we may regard those cells seen outside the blood-vessels as having been born *in situ* and not migratory, and thus as strictly histogenous leukocytes. These cells in both situations are actively phagocytic for bacteria, foreign particles, cell débris, and even for other cells (Plate III).

3. **Eosinophiles.**—The indications are that, like the polynuclear cells, these have their origin mainly in the bone-marrow. They are characterized by possessing most often a slightly lobate or horseshoe-like nucleus and by having in their cytoplasm relatively large refractive granules which take the stain with the acid anilin dyes. They are capable of migration, and are seen at an earlier period in areas of acute inflammation, though they are rarely in large and never in preponderating numbers. In some chronic inflammations of the skin they are found in greatest frequency. They have very rarely been observed to take up or contain bacteria, so that phagocytosis is not one of their active functions; they take no part in tissue formation. Certain powers have been attributed to them by Kanthack and Hardy [17] and others in connection with their characteristic granules, but these have been wholly denied by others, and nothing certain can be stated at the present moment. In peritoneal inflammation, as pointed out by Opie,[18] they are to be found accumulated in enormous numbers in the omental capillaries undergoing diapedesis.

The Fixed Tissues.—If one attempts to take a bird's-eye view of the body which has in one part an area of inflammation, there can be seen indications of a division of labor. The blood and its contained parts, especially the leukocytes, are depended upon for the supply of antitoxic and antibacterial substances which they bring from the body at large and convey from even remote tissues; but the affected tissue itself clearly plays a part. Success or non-success of the earliest movements against the invading irritant depend largely, if we may so express it, upon the garrison present at the time of the outbreak, and this garrison is formed essentially of the stroma cells; upon these depend primary phagocytosis and neutralization of the irritant; upon these depends also the restoring of the *status quo* after the acute part of the struggle is over.

It is most important to understand the immense local importance of this factor, the stroma cells. Where the irritation is of mild grade, these may show signs of proliferation from the very first. Thus in the very mildest grade, repair may be brought about without any leukocytes being attracted to the part; with greater severity of irritants these cells are destroyed at the center of greatest intensity. At the same time, at the periphery we find that lesser concentration of the irritants leads to activity on the part of these cells, to phagocytosis, growth, and proliferation. The higher the tissue cell, the more easily is its function disturbed or the less its power of proliferation or reproduction. The common ordinary connective-tissue cell is less sensitive and more resistant than are the migrated leukocytes; so that in a lymph gland, for example, under acute inflammation one may see the leukocytes broken up and fragmented, and behind these, as it were, is the solid wall of proliferated connective-tissue cells, not only resisting attack but even attending to and disposing of the dead and wounded leukocytes. They form the real backbone of the army in activity.

It is from these, in the main, that the new reparative cicatricial tissue is produced. We say in the main. But a few years ago we should have said entirely; now the pendulum has swung back somewhat, and with the recognition of the existence of histogenous leukocytes it is believed that some at least of these not directly developed at the site of injury may take a part in the process. That the preëxisting cells of the part are the main factors in the new growth is proved by the fact that this new growth never occurs in isolated areas away from preëxisting tissue, but always is in direct connection with that tissue.

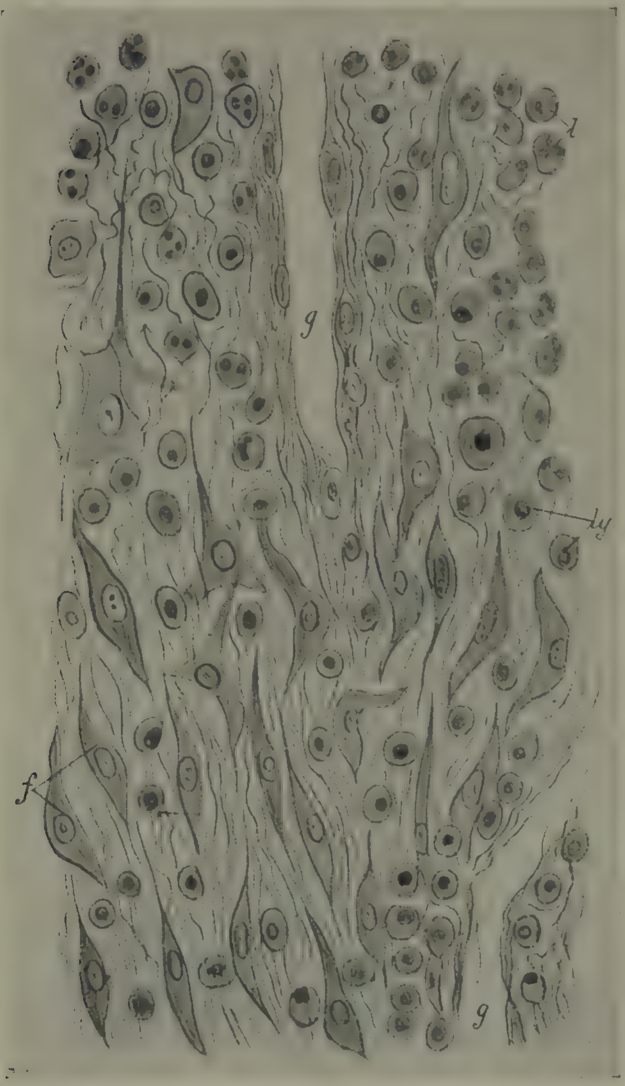


FIG. 37.—GRANULATION TISSUE SEEN FROM THE DEEPER TOWARD THE UPPER SURFACE.

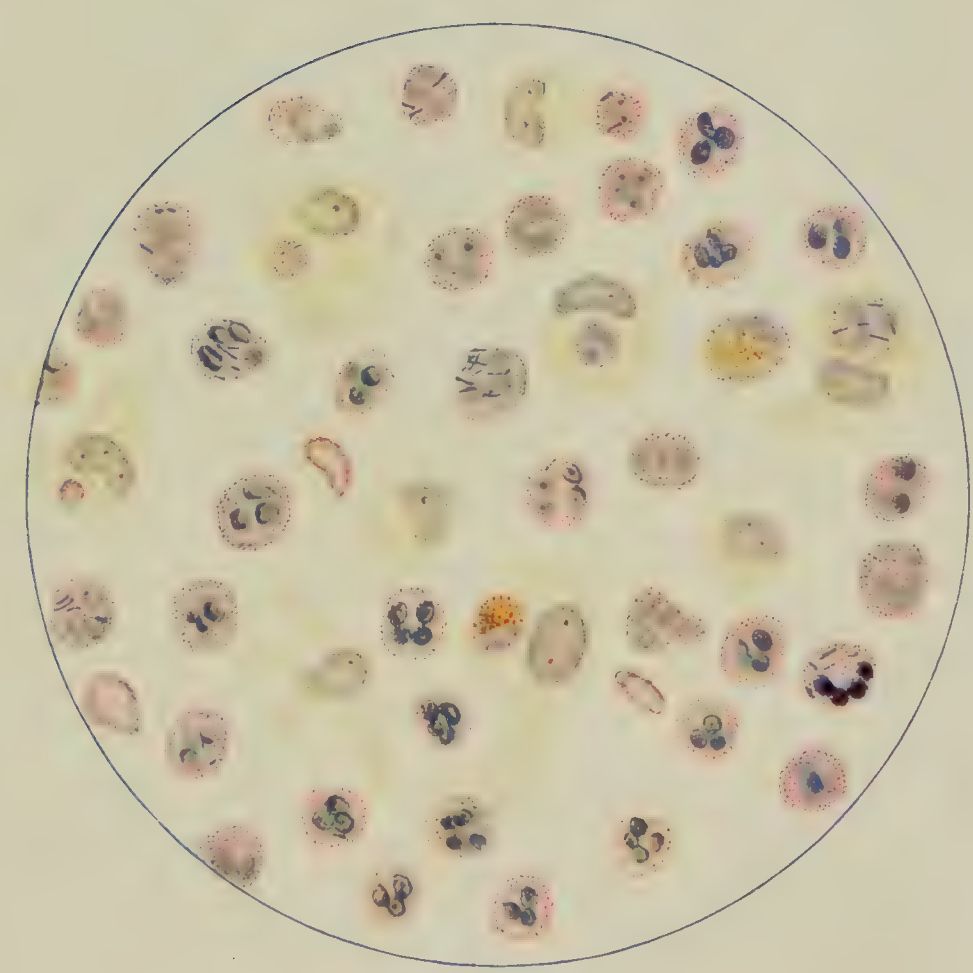
f, Spindle-cells, most abundant in deeper portions, where they are also becoming swollen; *e*, polynuclear leukocytes, most abundant toward outer surface; *ly*, lymphocytes; *g*, capillaries (Ribbert).

It may be said that in any inflamed area there appear three kinds of cells which we can distinguish, some of them obscurely, and which we are liable to confuse, and this because we are apt to encounter what appear to be transition forms: (1) First, the mononuclear cells referred to above in speaking of the lymphocytes, cells which are generally supposed to come from the blood, accurately resembling the mononuclear cells that do appear in the blood; second, cells which vary from oval to spindle shape, of different sizes, possessing a relatively large amount of cytoplasm (the fibroblasts), which can clearly be seen to give origin to the new connective tissue; and, third, cells rounded or polygonal, which we may speak of as the transitional class, which in the main we believe to be of tissue origin: among these are cells described under many different names.

We may discuss these three a little more fully.

1. **Mononuclear Cells.**—These occur in large numbers in non-fatal inflammations of serous surfaces, notably in the peritoneum (Plate IV);

PLATE IV.



Peritoneal Fluid Twenty-four Hours after Injection into Peritoneal Cavity.

Showing relative proportion of polynuclear leukocytes to mononuclear cells, pseudopodia of mononuclears, bacilli ingested by polynuclear cells, phagocytosis of polynuclear cells, eosinophiles and red blood-corpuscles by mononucleated cells, and digestion of polynuclear in mononuclear cells (Beattie).

(From the "Journal of Pathology and Bacteriology").

are the hyaline cells of Kanthack and Hardy; are stated by some observers to be derivable from the lymphocytes, though this is still a matter of doubt; have been definitely seen to develop from the endothelium of serous surfaces, and resemble the large mononuclear cells of the blood. They are actively phagocytic to other cells, as again to bacteria, and often show vacuolation. They are the macrophages of Metchnikoff and have been studied by Ruffer[19] and Mallory[20] in the lymph glands, where clearly they are of endothelial origin. Closely allied to these, if not identical, are the wandering leukocytes observed by Ranvier, Marchand, and others, which are sometimes termed "epithelioid" leukocytes. Here too we may include the cells newborn from corneal corpuscles, as studied by Council-

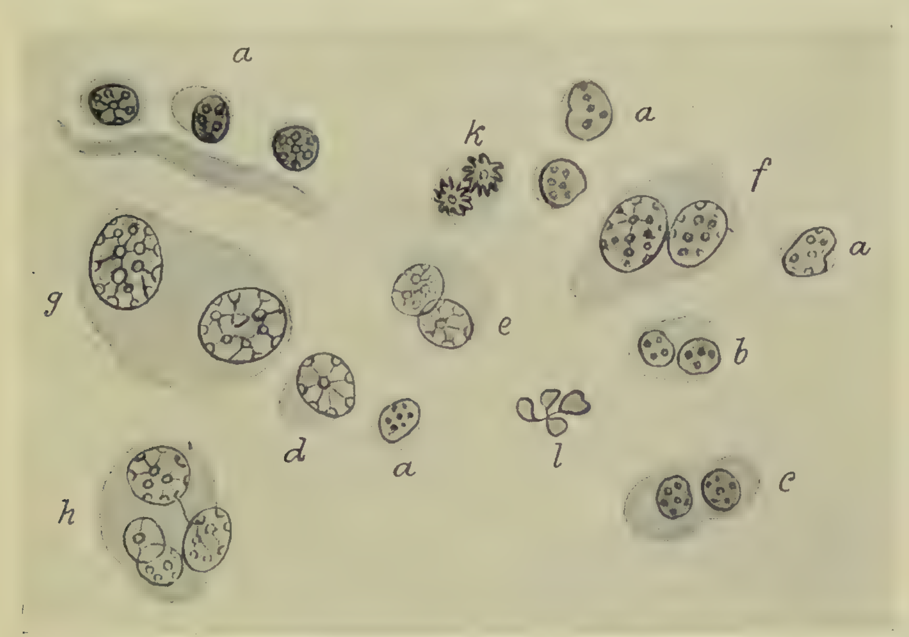


FIG. 38.—DIFFERENT FORMS OF PLASMA CELLS AND SO-CALLED LYMPHOCYTES FROM GRANULATION TISSUE (Marchand).

a, *a*, Lymphocytes; *b*, binucleated cell; *c*, cell recently divided; *d*, small round cell with larger nucleus; *e*, *f*, *g*, *h*, varying arrangement of nuclei.

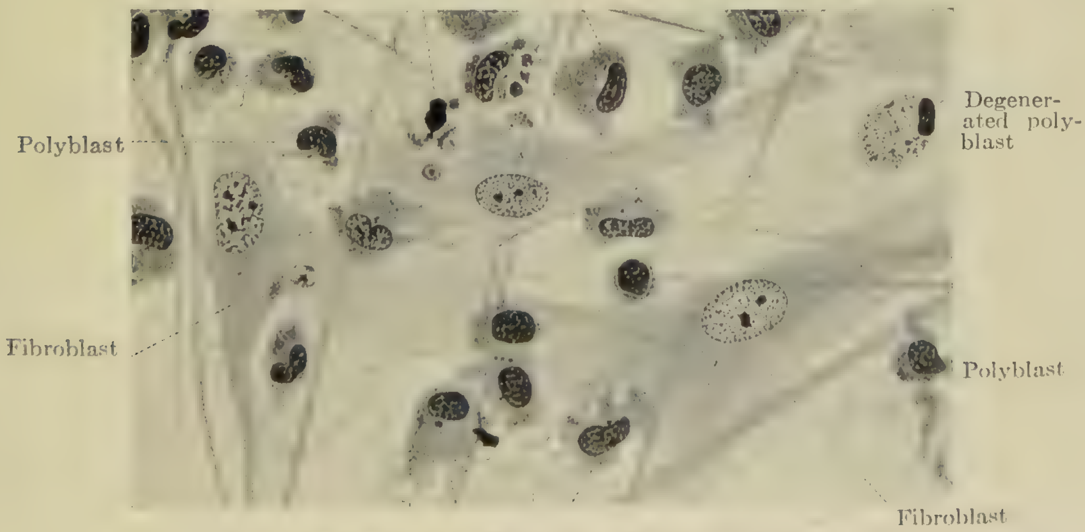


FIG. 39.—DEVELOPING CONNECTIVE TISSUE (Maximow).

man and others, and the free cells given off from connective-tissue cells or even from organized tissue, such as muscle, studied by Metchnikoff, Griffiths, etc. Some of these definitely give rise to new tissue cells, and although in the process of acute inflammation many are seen to disintegrate, we may suppose that as a class they can potentially form new tissue.

2. Fibroblasts.—The fibroblast must be regarded as a histoid cell in the stage preceding its adult fully formed condition. In some cases the evidence appears to be clear that these cells have been directly derived by mitosis, or sometimes by direct nuclear division from the connective-tissue cells of a part. These new cells, from being rounded, gain processes at either pole, become elongated. and spindle-shaped, and their processes join with fibrils from surrounding cells (Fig. 39). From these processes and from the sides of the cell fine wavy connective-tissue fibrils develop and eventually tissue indistinguishable from the fully formed normal connective tissue is thus produced.

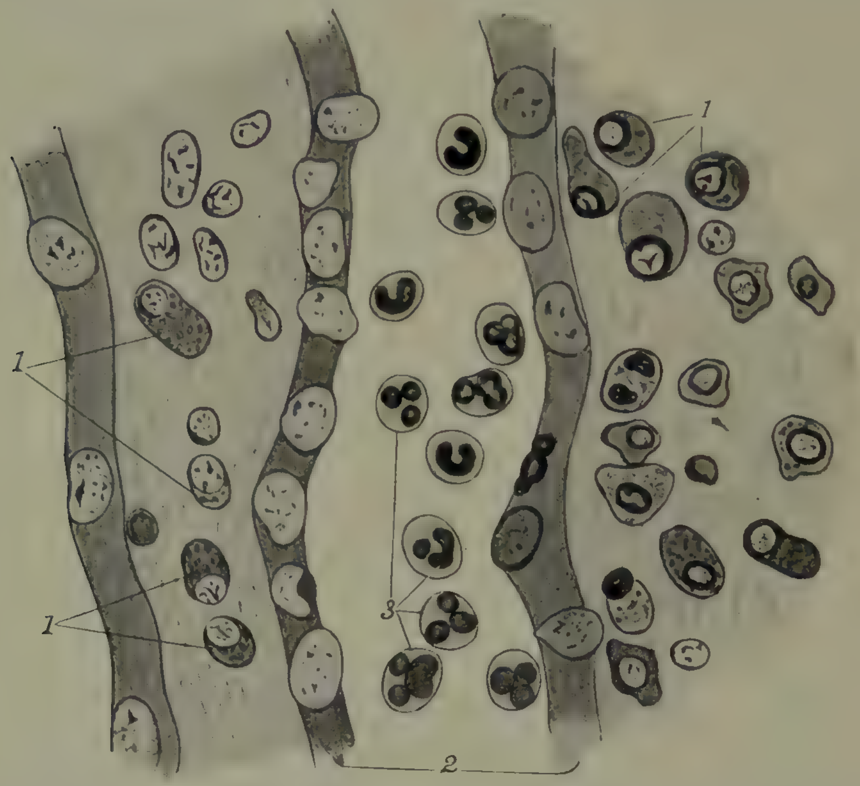
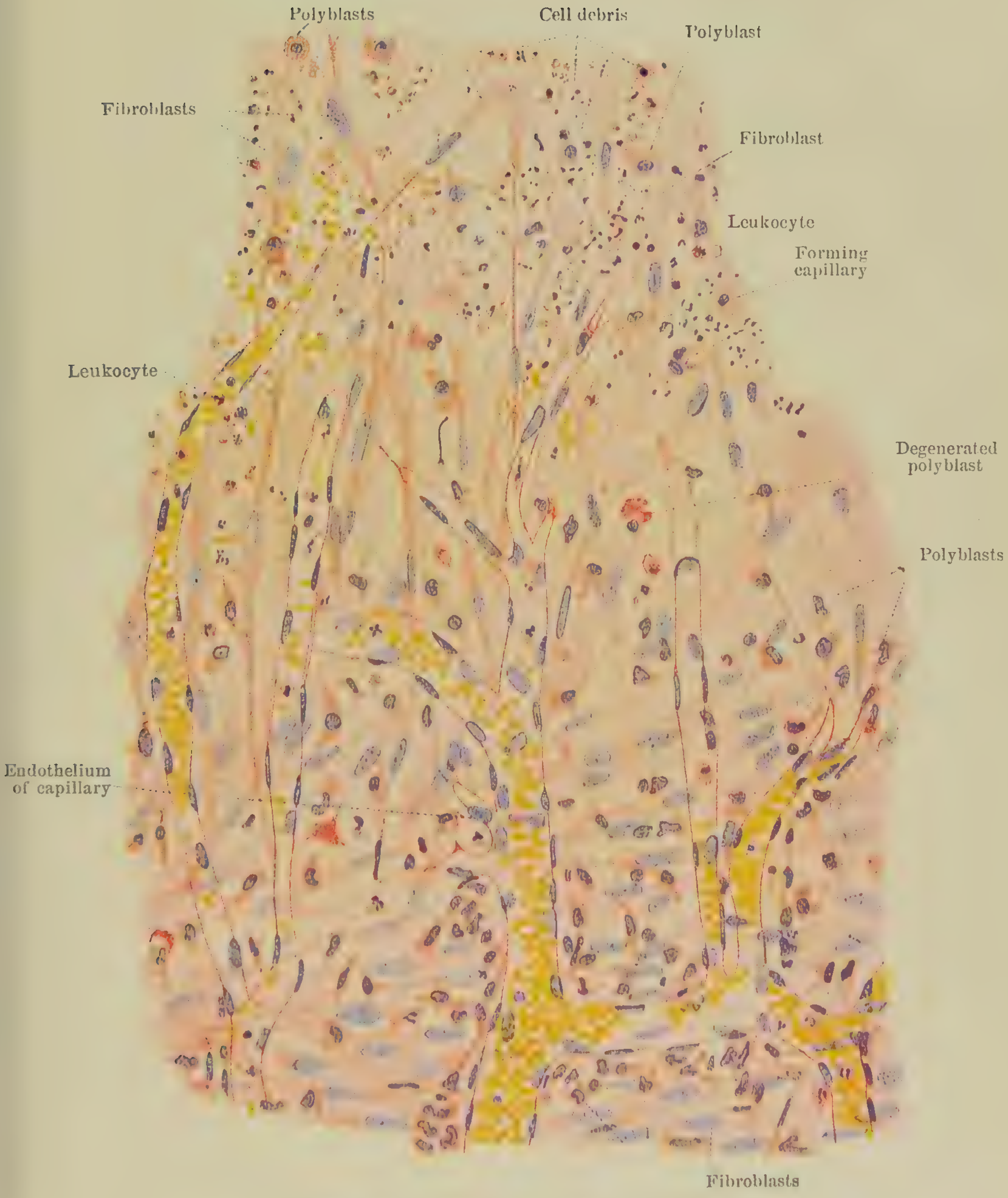


FIG. 40.—FROM A CASE OF ACUTE INTERSTITIAL NEPHRITIS (MAN), DRAWN BY CAMERA LUCIDA ($\frac{1}{12}$ Zeiss, ocular).

2, Showing plasma cells, (1) in the interstitial tissue between the tubules. The epithelium of the middle tubule (2) is degenerated; the tubule contains polynuclear leukocytes (3) (Councilman).

3. Free Cells Presumably of Tissue Origin.—We now come to the debatable class, which includes a bewildering series of cells described by different authors: the "plasma cells" of Unna, and of others who may or may not refer to the same cells as Unna; the "clasmatocytes" of Ranvier, so called because of the readiness with which they drop off remnants of their protoplasm; these, again, appear to be the cells that Marchand has called "leukocytoid cells." There are many described cells

PLATE V.



Developing Vascular Tissue (Maximow).
Growth is proceeding from below upward

which cannot be placed at all definitely, but it can be said in a general way that they all have certain features in common: they vary in size, sometimes attaining large dimensions; they have amœboid movement; they are phagocytic for other cells, for foreign particles, red blood-corpuscles, and less actively for bacteria; their chemiotaxis is of a low degree (Fig. 38).

In such a confused field Maximow[21] appeals strongly to us when, in addition to the definite hematogenous leukocyte and equally definite fibroblast, he includes all the above mononuclear cells under the designation of "polyblast." (Figs. 39, 41, and Plate V.) In view of the likelihood that many observers are describing under different names the same order of cells, it is a step in the right direction when he simplifies rather than amplifies our terminology. Not all the polyblasts go to form new fibrous tissue: sometimes they fuse together, forming giant cell masses, sometimes they wander away, some doubtless grow old while still in their wandering condition in the tissues, and disintegrate. When division of the nucleus occurs, or with cell fusion there is apparent nuclear multiplication, it is generally admitted that the cell or cells concerned are undergoing retrograde changes and have no part in tissue up-building.

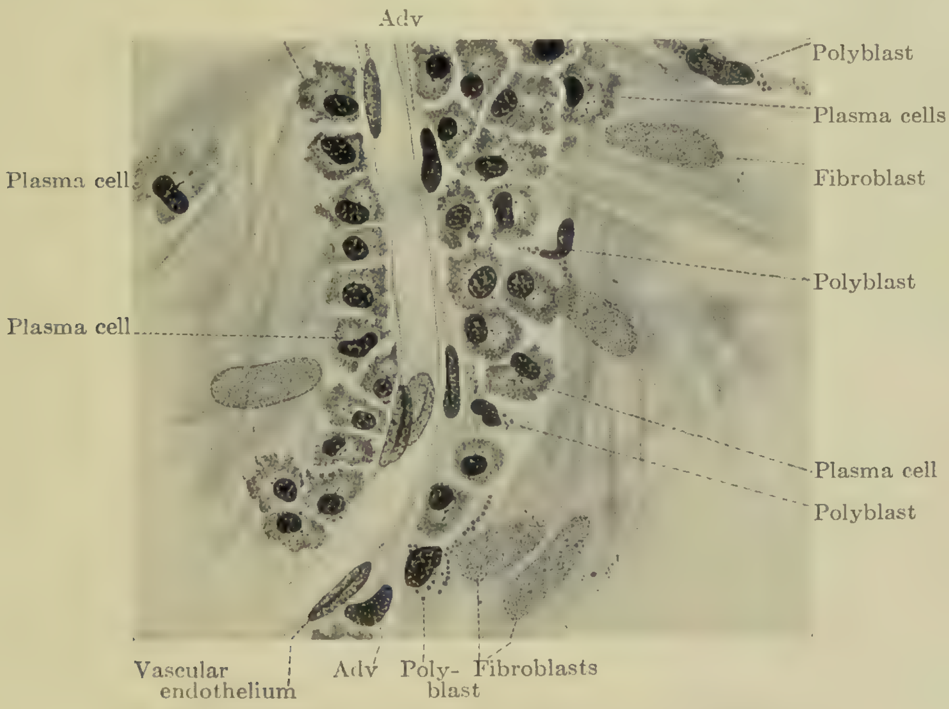


FIG. 41.—PERIVASCULAR GROUP OF PLASMA CELLS (Maximow).
Adv, Polyblast differentiated as an adventitia cell.

The Nerves.—The immediate effects of irritation upon the nerves and nerve-endings in the inflamed areas are largely unknown. We have taught in the past that the increased tension brought about by the exudation, and so the pressure upon the nerve-endings, was the immediate cause of pain. In the light of Schleich's observations upon the effect of distending the subcutaneous tissues with physiologic salt solution, and other innocuous fluids, this teaching must be given up. Increased tension in the part has an anesthetic rather than a pain-producing effect.

We must thus, it seems, fall back upon the chemical action of the toxins upon the nerve-endings as the main cause of pain.

We have already referred to the problem of the part played by the vasomotor nerves in connection with the vascular dilatation, and have shown that potentially the central nervous system can directly control to a considerable extent these vascular changes, although identical changes may take place in an area wholly cut off from central nervous influences.

In the case of nerve bundles having interstitial tissue and binding the fibers together, this tissue undergoes the changes common to connective tissue elsewhere, and the nerve itself may become swollen and infiltrated by cells of inflammatory origin.

INFLAMMATION OF SPECIAL AREAS.

1. Non-vascular Areas.—The study of these areas, such as the cornea, is well worthy of note, because we are able, by modifying the means of irritation, to prevent the occurrence of certain incidents, and to recognize a simpler type of inflammation than that accompanied by changes in the blood-vessels. In the very simplest form of irritation we find no leukocytes at all; injury of the external layers—for example, by chlorid of zinc—without rupture of the same, is followed merely by necrosis of the outer cells implicated, and prompt repair by proliferation of their neighbors. If the superficial layers be eroded, leukocytes accumulate in the wound, but these leukocytes have not made their way from the vascular system—at least, not directly—but pass thither from the lacrymal secretion bathing the cornea. If cocci be injected, after some hours the veins at the periphery of the cornea are seen to undergo dilatation, and now more abundant leukocytes make their way to the site of injury from the vein; repair is instituted, as before, by the corneal corpuscles and by the peripheral blood-vessels, which send in new branches. It must be remembered that while there is not actual blood-supply directly to the normal cornea, its tissue is bathed by lymph through abundant lymph channels; this lymph may be the source of some of the leukocytes making their way to the region of injury.

2. Of Serous Surfaces.—Hitherto in speaking of acute inflammation we have almost entirely referred to the process as it occurs in the depth of soft tissues; we have now to take into consideration the variation in the appearances in sundry other parts.

The serous membranes consist of a layer of endothelial cells lying above a somewhat highly vascularized subserous connective tissue. The membrane proper is thus, despite its importance, of very slight depth. So delicate is it that with inflammation its cells are very easily influenced, and large numbers of them become loosened and discharged with the exudate. That exudate and its contained cells, fibrin, etc., are products of change in the subserous layer. The very fact that the subserous layer is highly vascularized and that toward the free surface these vessels have very little support permits great, not to say undue, dilatation of the vessels and, as a consequence, in general, inflammation of the serous surface is accompanied by relatively abundant exudation.

So also in this order of cases there is a marked tendency toward the formation of fibrin; such fibrin does not show itself in normal lymph or serous spaces any more than it does in the blood under normal conditions. Just as thrombosis occurs in the vessel in which the endothelial lining has been destroyed, so in inflammation of a serous surface the casting off of the endothelial cells and the exhibition of, as it were, a foreign surface to the lymph, coupled with the increased migration of leukocytes, clearly favors this fibrin formation. We cannot but recognize that leukocytic disintegration sets free fibrin ferment and the precursors of fibrin.

But here, again, we may recognize at least two grades of intensity of irritation, the slighter leading to swelling and active proliferation and throwing off of the endothelial cells, the more severe leading to death of these cells and casting off of the dead cells. So also the most intense inflammations are characterized by abundant fluid exudate, the less intense by abundant migration of leukocytes, in milder and more chronic irritation by plastic formation and tissue overgrowth. We have in another section referred more fully to the part played by the fibrin which is so characteristic a feature of moderate grades of inflammation of serous surfaces.

3. Inflammation Affecting Mucous Surfaces.—The main distinguishing feature of the mucous surface is the presence there of a layer of mucous cells, cells of a glandular type, capable when stimulated of forming and discharging relatively large amounts of mucin. The hyperemia, the exudation of serum, the migration of leukocytes, all these occur in the submucosal layer just as in the subserous; the changes in the reaction are due solely to the interposition of this layer of mucous cells. There is, in the first place, a more definite basement membrane interposing a certain amount of resistance to surface exudation. The layer of mucous cells is more complicated, and although the fully developed cells may be discharged, they are apt to remain relatively undifferentiated "mother cells" at the base; or otherwise the same intensity of irritation does not lead to as extensive a denudation. And, thirdly, by the combined action, it may be, of the irritant and of the hyperemia the fully formed mucous cells are stimulated to produce increased amounts of mucin, so that an inflammation of moderate grade is characterized by the abundant amount of mucinous discharge rather than of fibrinous deposit.

We speak of such a moderate case, with exudation of serum containing abundant mucin, cast-off mucous cells, and relatively few leukocytes, as a "catarrhal inflammation"; if there be sufficient leukocytes extruded, the character is altered to that of a "mucopurulent inflammation"; if more severe, with complete destruction of the mucous membrane proper, with its cells and necrosis, then, as in connection with serous surfaces, there is the same tendency for the leukocytic exudation to favor a deposit of fibrin upon the surface, and then we obtain a "membranous inflammation."

Despite the fact familiar to all that diphtheria is a disease set up by a specific bacillus, and the equally well-known fact that a like membranous inflammation may be induced by several forms of microbes, we still commonly speak of such a membrane as being diphtheritic. It would be better to confine this term purely to cases in which we know that the Bacillus diphtheriæ is the causative factor; failing this, we may accept the term diphtheritic as covering all such membranous inflammation, and employ the term *diphtherial* for such cases as are of pure diphtherial origin.

Further, if there be yet more severe destruction of the surface cells, this may go on to ulceration. Where we have pyogenic organisms present, there is a dissolution and breaking-down of any fibrin that is formed and consequent absence of a membrane. In such cases there is a distinct tendency for the process to extend in the submucosa beneath the still intact mucous membrane the part becoming infiltrated with pus. This form is spoken of as "phlegmonous inflammation."

4. Inflammation in Lymphoid Tissue.—This important tissue deserves special note because we may regard it as the one tissue of the body in which inflammation is the rule rather than the exception. The lymph nodes stand between the body and the thousand little attacks that are made on it from many sources, so that in an adult a lymph gland that has performed its service is in a more or less damaged state; the strictly normal lymph gland can be found only in the very young.

Lymphoid tissue by its structure has a peculiar strength in resisting inflammation. Existing in large amount through the body, not only in the large lymph nodes but also in tiny collections of cells scattered through all the supportive structures (we must here include the medulla of bones), it represents a large bulk of tissue whose main function appears to be defence; not only does it actually defend, but it supplies anew the ranks of the defending blood-corpuscles: the polynuclears and the eosinophiles from the medulla of the bones, the lymphocytes from the ordinary lymph nodes. It is entirely mesoblastic, has no admixture of higher class specialized cells, has, as it were, no supplies to guard, and can apply its full force to attack and to defend. The lymphoid tissue consists of lymphocytes in great numbers lying in a stroma of connective-tissue cells, which stroma cells are the boundaries of the lymph spaces, and are themselves actively phagocytic, as already indicated. We must regard all these cells as the most able "fighters" that the body possesses.

The conditions prevailing in a lymph node subjected to an acute inflammation are those occurring elsewhere: there is dilatation of the blood-vessels, so that the node looks pink instead of gray; exudation of serum, so that the lymph-gland is succulent. Migration of leukocytes undoubtedly occurs, but the part is normally a mass of lymphocytes, and further migration may add to their numbers without our being able to appreciate the increase unless polynuclears come to preponderate. Actual increase of the cells in the part is difficult to follow; that it does occur is evident when a portion of a node is mechanically removed or destroyed. With all this there will be an enlargement of the gland, and it may be painful, but unless the enlargement be great our coarse methods of examination do not allow us to observe it. In a chronic inflammation of a gland, serous exudation and leukocytic migration being at a minimum, and tissue proliferation at a maximum, the ordinary result is enlargement with distinct fibrosis.

The outcome is that the microscopic examination of a lymph node is unsatisfactory for the purpose of defining moderate degrees of inflammation therein. The processes of suppuration and of resolution follow the same course as in other tissues.

5. Inflammation in Bone.—The dense structure of bone, cartilage, tendons, and allied structures modifies the process that occurs in inflammation in these parts precisely as would be expected. Bone is dense and resistant and offers little space into which exudation can occur, offers no elasticity to favor the swelling which is the natural result of inflammation. As a consequence any flushing or diluting action of the exudate is at a minimum, and if we ascribe pain to the action of toxin upon the nerve-endings we can understand why it is that frequently pain is severe.

Nevertheless the process is the same as elsewhere; there is the same migration of leukocytes and tissue destruction, although, from the unyielding character of the bony matrix, the breaking-down processes do not show themselves so rapidly. This same unyielding character is seen in tendons which may lie in necrotic tissue or bathed with pus; their very density protects them to a large extent against bacteria as against the solvent action of the products of the pus cells.

THE RESULTS, OTHER THAN LOCAL, OF INFLAMMATION.

Metastatic Inflammation. — Inflammation similar to that in the primary site may occur secondarily in different parts of the body by carriage of bacteria in the ways enumerated below. While it is a recognized fact that toxins of themselves can cause inflammation, and such can be produced experimentally, in the natural conditions of disease anything like restricted localized inflammatory reaction to such toxins is rarely recognized. Instead of this, we in general obtain diffuse degenerative changes, more particularly in the organs through which these toxins are excreted. These changes are certainly a reaction to the toxins; whether it is correct to speak of the swelling, cloudy and even fatty changes which do occur as a consequence (in the kidney, for example, as acute parenchymatous nephritis), changes which may be unassociated with any evidence of leukocytic migration, depends upon the empiric boundary we establish for ourselves between stimulation and irritation. The local changes that we may obtain in the lymphoid tissues of the body within twenty-four hours after the infliction of extensive burns, and the focal necroses seen in the liver in acute infections, are primarily due to such specific local action of toxins; similar changes, however, are not seen following upon a well-localized acute inflammation.

For the development of metastatic inflammation proper, it is essential that the bacteria setting up this primary disturbance be carried to the new site.

(1) Bacteria may be carried either free in the lymph or blood-stream or in leukocytes or phagocytic wandering cells, or with cellular material, as in septic emboli. If they are in a cell, the struggle is fought out once more: if the bacteria have the greater power of resistance, they multiply in the dying or dead cell body; if the cell win, they are destroyed. In the case of bacteria free in the body fluid, this struggle is likely to occur either in an endothelial cell of one of the vessels or often in a lymph node, and where the bacteria are not destroyed but multiply, the lymphoid tissue itself may be the site of the metastatic inflammation. In the other case, the bacteria are arrested in some small capillary, and, destroying the endothelium, block up this capillary and so become the center of inflammatory reaction and subsequent abscess.

(2) There may be stasis and subsequent thrombosis of the vessels at the site of primary inflammation, and the bacteria may grow into the coagulated blood and so spread along the thrombus.

(3) There may be extension of infection from one part of a serous cavity to another.

The two latter cases should perhaps be considered rather as extension of a primary inflammation than as true metastatic inflammation.

Results Upon the Body at Large.—During a severe local inflammation even without metastatic developments there is a constant stream of toxin-containing lymph and blood from the part, and this, circulating, bathes the body-cells, until it is excreted. Each cell so bathed suffers in a twofold way: its nutrition is poorer than usual and the toxin acts apparently as a stimulus leading to chemical changes and increased metabolism. This increased work shows itself in general increase of body-temperature and fever (though this is but one of the factors in the febrile state) and in increased excretion of metabolic products. Some cells, by reason of their function or of their position near the focus of inflammation, suffer more than others. We have already indicated that those which suffer most are the cells of the excretory organs, notably of the liver and kidneys. The very fact that the vital processes of the whole body are so finely adjusted and dependent one upon the other necessitates that disturbances in the excretory organs react harmfully upon every other part of the body; the irritation thus tends to be cumulative. It has to be remembered, further, that the products of modified cell metabolism act on the whole deleteriously, and are apt to throw increased work upon and so damage the cells of the excretory organs, just as do the products of the bacteria themselves.

SUBACUTE AND CHRONIC INFLAMMATION.

The terms acute, subacute, and chronic applied to inflammation are relative, and therefore arbitrary. A chronic inflammation is one which lasts long, an acute inflammation one of short duration. A subacute inflammation is one which falls into neither class; the term is a compromise. Thus far with regard to time. As regards intensity, we may have cases in which the toxin is so weak that the tissues react but slightly, have little influence on the vessel walls, and cause no pronounced attraction of leukocytes. If we were able to recognize the inflammation even three days after infection began, we would not therefore be justified in calling it acute. For all practical purposes the irritations that are as weak as in this supposititious case are prolonged; long duration and low grade of activity go hand in hand; such a case we should certainly class among the chronic inflammations.

Here attention must be called to a group of microbic irritants of a low grade of virulence, setting up chronic inflammations, having a certain family likeness, producing in general multiple localized foci of inflammation which have received the name of "infectious granulomata." These foci are characteristic of tuberculosis, syphilis, actinomycosis, chronic glanders, blastomycosis, etc. The very use of the term granuloma—a tumor of granulation tissue—implies that tissue overgrowth is a prominent feature in these cases; and such proliferation of the cells of a part is in all cases associated not with acute inflammation but with chronic or at most subacute conditions.

Here it deserves note that the term chronic is apt to be driven hard, and overdriven. Conditions of widely different nature are familiarly included under the one term. When we speak of a chronic inflammation we ought properly to indicate that inflammation is still in progress and is of such a nature that it has extended or is liable to extend over a long period. The results of a past inflammation ought not to be designated by this term. We should speak of such as old inflammation. So also repeated attacks of acute or subacute inflammation affecting the same area are apt to be included; it is more correct and at the same time more lucid to refer to these as "recurrent inflammation," under which heading may also be included the acute exacerbation of a previously existent chronic disturbance. Nevertheless we have to admit that from the morbid anatomist's standpoint it is often a matter of great difficulty to say whether a certain fibrosis be the result of an old acute or present chronic inflammation. In this very fact we have additional support for the position here taken that the distinction between acute and chronic inflammation is arbitrary.

As already laid down, we encounter every grade of irritation; on the one hand, we may have a bacterial infection so acute that in the course of a few hours there may be produced a necrosis of all the elements of a tissue; on the other hand, grades of irritation so low that months and it may be years are required to bring about definite results. Such a condition, for example, is cirrhosis of the liver. We do not admit that the differences between these two extremes are anything but differences of degree, but just as the predominant feature of an acute inflammation may be exudation of serum or migration of leukocytes, so the predominant feature of a chronic inflammation is essentially tissue overgrowth, and more particularly overgrowth of the least differentiated elements of a tissue. Even in the lowest grade of inflammation it is probable that there is always some dilatation of the blood-vessels, some migration of leukocytes, some increased exudation; but these may be so slight as to pass unnoticed in comparison with the cell proliferation. It follows that a toxin of this low grade sets up correspondingly slight systemic disturbances.

There are certain features characterizing chronic inflammations that demand passing notice, more particularly giant cell formation and certain necrotic changes. The giant cell when found is essentially an accompaniment of chronic disturbance. When it occurs in a foreign body inflammation, this cannot be regarded as an exception to the rule, for the foreign body is the least active of all the causes of acute inflammation, leading not so much to great exudation and diapedesis as to tissue production. In other forms, which we may class as acute inflammations, the giant cell shows itself only in the later reparative stage. It may be found enclosing or surrounding shreds of elastic tissue[22] or crystals of cholesterin (Lecount[23]). It is in the infectious granulomata that it is oftenest found, most frequently in tuberculosis, less frequently in the other forms.

While there is another form of giant cell seen in non-inflammatory states, a form due evidently to multiplication of the nuclei of a cell without subsequent division of the cell body, the form seen in inflammation is strictly comparable to the plasmodial aggregation and fusion of cells around a foreign body in the invertebrate cœlomic cavity; it consists of a fusion, temporary or permanent, of proliferated mesoblastic cells of connective-tissue (including endothelial) origin. It takes no part in tissue formation, although the constituent cells have occasionally been observed in what seems clearly to be the process of separation[24] and the separated constituents may possibly take on one or other of the activities proper to other cells of connective-tissue origin. Most often it disintegrates and disappears; it has been observed to have definite phagocytic power—tubercle bacilli, for example, in various stages of disintegration have been observed within these giant cells. And in the center of the giant cell mass in these and other cases is often necrotic material.

With regard to the second point of similarity, it must be noted that the tendency to suppuration and necrosis is common to all acute inflammations. It is rare in chronic inflammations save in the transitional class, the subacute infectious granulomata. At bottom caseation, the formation of gummy material, and the oily débris seen in the center of the granuloma in tuberculosis, syphilis, and chronic glanders respectively, are identical with the tissue dissolution that occurs in an acute abscess. The essential cause in each is the action of a specific toxin, each toxin having its particular method of acting upon and disintegrating the cells.

THE TREATMENT OF ACUTE INFLAMMATION.*

It is not so much a part of our duty in this chapter to define the practice of the surgeon in a particular case of inflammation as to refer to the general principles which should govern treatment, and to indicate broadly how modification in the circumstances necessitates variations in procedure. To these differences between individual cases we have repeatedly referred, and to the causes underlying the differences. Theoretically—and practically—there is no one mode of procedure. Even in an individual case the treatment must vary according to the stage of the disturbance.

Naturally old prepossessions, long acted upon, are difficult to displace. We are prepared to find that many a surgeon will adhere to the teaching received in youth that inflammation is dangerous, is in itself a harmful process, and must be counteracted. This older teaching cannot be harmonized with the successful practice of today: with the purposeful exaggeration of processes which are part and parcel of the inflammatory manifestation—with von Mikulicz's application of Issaeff's "resistance period" to assure increased leukocytic activity, or with Bier's greatly extended employment of passive hyperemia to counteract acute disturbances.

Inflammation is a danger-signal, but by no means necessarily a danger. Wherever we observe the outward and visible signs of inflammation, we have the indications that something abnormal has occurred in the tissues, something which has brought about a reaction on their part. In approaching a given case the first question that the surgeon has to ask himself is, What is the probable cause of this reaction? the second, How is this individual case to be treated? And as regards treatment he must recognize that there are before him alternative and, in practice, widely different methods. He must determine which in the particular case will insure the speediest and most thorough return to or toward the normal. Nature teaches this to the lower animals and to man through the influence of pain. It is the surgeon's duty to recognize the importance of this teaching and to adopt such means as shall be adequate. The inflamed joint should be given physical rest by immobilization, and the inflamed retina physiologic rest by the exclusion of light. Physical and physiologic activity of injured and inflamed tissues interferes with nature's processes of repair and predisposes to an extension of the involved area.

Position is often of importance. The elevation of the limb may be a very essential element in the treatment of an inflamed leg. It is a well-known fact that emptying the veins of a limb by elevation leads to reflex contraction of the arteries.

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* While I am responsible for the broad outlines of this section upon treatment, and have endeavored to make it the logical outcome of the considerations brought forward in the preceding portions of this chapter, as a pure pathologist, not in practice, it would be presumptuous, not to say dishonest, for me to pretend to lay down practical details. My colleague, Dr. G. E. Armstrong, has here most kindly come to my aid, and has afforded throughout the section such data as seemed necessary, it being held by both of us and by the editor that more minute details should be sought in subsequent chapters upon regional surgery; that, in short, what is found here should be merely the broadest principles of treatment.

(1) Removal of the noxa or irritant, or (2) guidance of the reactive process of the organism, so that without operative interference the irritant shall be neutralized and destroyed, are rival methods of treatment worthy of consideration.

1. Operative Interference.—Time and again, and wisely, the first of these procedures will recommend itself to the surgeon. Even under favorable conditions the methods of nature are leisurely, the reaction at first too often inadequate, so that, more particularly in bacterial inflammation, the essential cause of the disturbance is given time to grow and to extend beyond the original focus, whereby the condition becomes unduly generalized; and even if eventually the microbes be neutralized and destroyed, the reparative processes over the larger area, the formation of cicatrices and adhesions, may be so extensive as to produce deformity, arrest of action of parts, and yet graver sequels. And where microbes are not primarily responsible, operation is often demanded. An extensive hemorrhage into a part, with liberation of the proteids and enzymes of the blood-cells, is followed by all the symptoms of inflammation. The natural absorption of blood out of place is a slow process, and, although in the absence of infection the tendency is toward complete absorption, there are conditions of extensive hematoma in which it is better to remove the irritant than to wait. The same is true of sequestra and all dead tissues, which so long as they remain are a source of irritation and only slowly undergo absorption; and so long as they remain, should the reactive process of the individual become lowered, they afford a *locus minoris resistentiæ* and may become a focus of infection even although unconnected with the exterior. This applies also to exogenous foreign bodies. They are sources of irritation and reaction on the part of the surrounding tissues, and are in general better removed than allowed to remain, although the more inert they are, the less the extent of the irritation. So that in the case of projectiles, for example, practice must be in part determined by the supposed position of the foreign body.

One more indication may be here laid down, namely, that in conditions which have passed from being purely localized to becoming generalized the removal of the primary focus is frequently advisable. Thus, it has been noted in connection with tuberculous peritonitis that laparotomy is most often followed by good results if it be accompanied by excision of the mesenteric glands, the Fallopian tubes, or other tissues which show signs of the most advanced and oldest tuberculous change. So also it has been repeatedly observed that in anthrax, when already general febrile symptoms have become prominent, removal of the primary malignant carbuncle—some say only of a portion of the same—may be followed by recovery.

It is obvious that in a general article all particular cases cannot be passed in review. This may be laid down, that where the indications are that free excision of the inflammatory focus can be accomplished with reasonable expectation of thereby removing satisfactorily the cause of the condition and without undue injury to other tissues, or subsequent disfigurement, excision is to be recommended, or, what comes to the same thing, scraping out the focus or destroying the irritant by caustics, irrigation, antiseptic solutions, and the like.

2. **Promotion of the Reactive Processes.**—But this is not always possible. For cosmetic reasons, free opening may be objectionable: the part may be so situated that the prevention of infection from without—after excision—is difficult to guard against; the inflammation may be so extensive and the inflammatory agent so virulent that grave danger exists that the act of operation, instead of wholly removing the irritant, may lead to its spread into previously healthy tissues.

Then, again, there is another class of cases which has to be considered—a class which we assuredly must consider as inflammatory in the terms of our definition. We refer to the acute reactions which follow physical and mechanical injury in which there is injury of the tissue with displacement of parts; prominent in this class are simple fractures and sprains. In these, beyond such procedures as are necessary to bring the parts into proper relation, there is no thought of operative exploitation of the injured areas. Under all these conditions the advantages of the other form of treatment have to be weighed, and preference given to means of promoting the local inflammatory reaction, in the hope that thereby the tissues and fluids of the body will be able to neutralize and destroy the irritant agent or condition and bring about return to the normal.

Coming now to consider how this may be brought about in any individual case, it is before all things necessary to bear in mind the extent of reaction already exhibited. As a matter of fact, the reactive processes may be:

(i) Inadequate to neutralize the irritant and bring about repair.
(ii) Adequate for these purposes.
(iii) Excessive.

And this either as a whole or in some one or other direction. There may, for example, be excessive hyperemia and exudation of fluid with deficient leukocytic migration.

Obviously the treatment of these different grades must be radically different, and it is of prime importance for the surgeon to determine which of these three he has before him.

(A) **Adequate Reaction.**—For more convenient handling we will discuss these in a different order, and first dispose of the cases in which the reaction is adequate. These cases obviously require no local treatment; they are the cases which, as a consequence, sundry surgeons, starting from the prepossession that all inflammation demands treatment, object to include in the category of inflammations. It is, as I have pointed out, both logical and essential so to include them. Such are the conditions accompanying the natural healing of fractures, the healing of incised wounds, whether surgical or otherwise, etc., conditions accompanied by a moderate grade of localized redness and swelling and exudation without pus formation and with little pain, with evidence, that is, of irritation of so mild a grade and so lacking in progressive increase that at the end of twenty-four hours or so the reaction has reached its maximum; cases, in short, in which, the general health and power of resistance being satisfactory, the local reaction is rapid. The practised surgeon intuitively recognizes cases of this order; nay, more, his object is to bring every wound and injury into such a state that this, which we may term the natural reaction, may be attained. To this end it is that he renders the wound aseptic; that he brings incised surfaces into apposition; that he removes foreign and dead matter. Once he attains this adequate reaction, no further local measures are necessary—general measures alone may be employed. He has to recognize, that is, that the adequacy of the local reaction is the expression of and depends upon the healthy condition of the blood, and to a certain extent of the nervous system, and that these in their turn are the outcome of healthy coördination of all the component parts of the organism as a whole. To attain and to preserve a healthy local reaction it is necessary to see to it that more particularly the bowels are properly regulated and the kidneys working well. We shall in a later paragraph deal more fully with these general measures.

(B) **Inadequate Reaction.**—Notwithstanding the fact that in this order of cases the evidence of reaction is most pronounced; that the redness, tense swelling, heat and pain, and general bodily disturbances are such as to direct attention to the severity of the condition, and that the disturbance is found to be extending, and that so the first impression is that these are examples of excessive reaction, the majority of cases of acute inflammation, cases which from their symptoms call for interference, are truly examples of inadequate reaction: the forces which the organism has been able to oppose to the irritant have been insufficient to neutralize it. And if local incision or excision be contraindicated, the rational treatment in such cases is *not to seek to reduce the inflammatory manifestations, but, on the contrary,* convinced that these in the main are beneficial and are means whereby the organism antagonizes the noxa, *to promote and increase the same,* recognizing that thereby the chances, on the whole, are distinctly greater that the irritant matter will undergo local destruction than that it will be afforded the opportunity to become generalized.

Recognizing this principle, it is interesting to observe how, empirically, generation after generation has acted upon it. The poulticing, hot applications, and retention of heat in the part, and all the various means employed to bring an inflammation to "a head," are one and all methods tending to induce a greater determination of blood to the part: the so-called "counter-irritants" applied locally are shown by more recent studies to be nothing of the kind.[25] Instead of causing a superficial hyperemia, and so lessening the congestion in the deeper inflamed area, they are found to cause a diffuse widening of the vessels, so that, for example, branding the skin over the vertebral column on either side, instead of blanching the cord, brings about pronounced local hyperemia of the same.* Even Ambroise Paré, as Bier points out, had noted the good effects of compression applied to a limb above and below a fracture in hastening union of the parts, and independently von Dumreicher [26] and Thomas, [27] of Liverpool, in the seventies and eighties of the last century, had called attention to the same. In addition to this "damming," Thomas employed active percussion with a hammer over the broken ends in cases of delayed union as a further means of stirring up the inflammatory reaction. The results reported by him were excellent.

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* I am doubtful whether the researches upon the matter of counter-irritation are as yet complete. I should not be surprised to find that while strong surface irritation by heat, severe vesicants, etc., has a direct congestive effect upon the deeper vessels, milder grades, by inducing only a superficial hyperemia, may, to a slight extent only it is true, lessen the congestion in a deeper part. That an

More recently other processes of augmenting the inflammatory reaction have had their adherents. Thus, Woodhead and others yet earlier have found that the spread of erysipelas is arrested by painting the skin with a caustic, such as silver nitrate, some three-quarters of an inch or more in front of the advancing margin of the reddened area. By this means a local subcutaneous inflammation is set up beneath the zone of treatment, so that when the organisms of the disease spreading along the lymphatics reach the zone they are destroyed by the phagocytic and other activities of the migrated leukocytes. There is provided thus an adequate and timely reaction. The frequent failure to obtain results by this procedure is, I believe, due, as Woodhead pointed out, to non-recognition of the fact that streptococci are present in the lymphatics at least half an inch in front of the edge of the reddened and swollen area, and that the painting must be well beyond this. Similarly, as I pointed out some years ago,* the method which has so frequently been found successful, of arresting peritoneal tuberculosis by simple laparotomy—by opening the abdominal cavity, removing any fluid present, and closing up again—obtains its most satisfactory explanation in the inflammatory reaction which follows. The reaction previously had been inadequate; the additional hyperemia and leukocytic migration induced by the laparotomy suffice to turn the tables in favor of the tissues and against the tubercle bacilli. We doubt not that it will be found that in a majority of cases the mere intraperitoneal injection of blood-serum or salt solutions, repeated at intervals, will have the like beneficial effect.

The reader will call to mind yet other instances in which, either empirically or with a recognition of the value of securing an adequate reaction, he has employed methods of bringing about an increased inflammation in order to accomplish a more speedy cure.

Two important recent advances in treatment directly along these lines must here more particularly be mentioned: I refer to von Mikulicz's preparatory intraperitoneal injections prior to abdominal operations and to Bier's promotion of passive hyperemia in the treatment of acute suppurative, tuberculous and other conditions.

In 1894 Issaeff [28] noted that the intraperitoneal injection of relatively

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area of intense congestion tends to be surrounded by one of correspondingly intense anemia I do not in the least believe.

*Adami: "Montreal Medical Journal," 1895, xxiv, p. 302. It may be of interest to quote the conclusion of ten years ago: "We may therefore, I think, safely state that when laparotomy is successful in bringing about an arrest of peritoneal tuberculosis, it achieves this result as a consequence of the increased activity or reaction of the tissues—of the cells forming or going to form the tubercle—induced by the simple inflammation set up."

bland noxæ, such as saline solution, serum, or urine, is followed by what he termed a "resistance period," beginning a few hours after the injection and lasting for at most five days, coinciding in this with the appearance and continuance of a marked intraperitoneal leukocytosis. During this period what in the untreated animal would be fatal doses of pathogenic spirilla might be injected with impunity; the abundant leukocytes already in the field take up and destroy the bacteria, whereas otherwise these same bacteria would have multiplied to such an extent, before producing sufficient toxins to stimulate leukocytic migration, that the tardy leukocytes would never have been present in sufficient quantities to engulf and destroy the proliferated bacteria.

In 1897, Durham,[29] of Cambridge, amply confirmed the existence of this resistance period of Issaeff, and found that it applied to pathogenic microbes in general. Some years elapsed before the practical value of these observations was realized by the surgeon. Then in 1904, with his characteristic thoroughness, von Mikulicz [30] took up the matter, determined again experimentally the phenomenon in question, and proceeded with enthusiasm to develop a method of intraperitoneal injections preliminary to abdominal operations upon aseptic cases. This with the object of guarding against peritoneal infection following upon the operation. Following von Mikulicz, Borchardt[31] has been able to protect guinea-pigs against two to three times the fatal (intraperitoneal) dose of B. coli. Von Mikulicz employed dilutions of nucleinic acid. Adolf Schmidt [32] has noted that physiologic salt solution in fair quantities is equally effective, and records good results in five cases of laparotomy. In these he employed a mixture of horse serum and salt solution, introducing it into the abdominal cavity by means of a trocar some nineteen hours before operation.

There is no reason why this previous or anticipatory treatment of possible infective inflammation, this casting out of Satan by Beelzebub, should not in the near future be employed in connection with operations in regions other than the abdominal cavity.

While to Bier cannot assuredly be given the credit for first recognizing the value of increasing the inflammatory reaction by increasing the hyperemia in the already inflamed area—for, as already indicated, quite a series of surgeons had made the observation in earlier generations—to him must certainly be given the credit of giving to this a leading rôle in his practice, and, what is more, of calling the attention of other surgeons to its value in no uncertain tones. Bier was directed to the employment of hyperemia as an agent against tuberculosis by the observations of Farre, and Travers (1815), Louis, (1826), and Frericsh (1853), that there was a noticeable coincidence of pulmonary tuberculosis and pulmonary stenosis, and the presumption that the development of the former was due, in part at least, to the pulmonary anemia resulting from the lesion. The contrary proposition was stated by Rokitansky in 1838, namely, the absence of tuberculosis, especially pulmonary tuberculosis, when mitral stenosis with its resulting pulmonary hyperemia obtained.

Bier employs increased hyperemia obtained by divers methods for divers purposes. He employs both active and passive hyperemia. The active he obtains in the main by the local application of heat, notably by hot air (in this his apparatus preceded the Tallerman machines and the various modifications of the same which have been recommended from so many quarters during the last few years). Such active hyperemia, with more active flow of arterial blood through the parts, he finds to be the more useful in chronic cases, or, more exactly, in promoting the absorption of the products of old inflammation. It is serviceable in acute cases, but not nearly so useful as is passive hyperemia brought about either by compression so applied as to obstruct temporarily the efferent veins of a part, without arresting the entry of blood through the afferent arteries, or by suction, either by cupping glasses in cases where the inflamed area is small and superficial, or by glass chambers into which the affected part can be introduced and the surrounding air rarefied by means of suction.

This is not the place to enter into the details of Bier's treatment—these will be found in his work on this subject.[11] Suffice it to say that the hyperemia produced must not by any means be so extreme as to lead to a white edema of the part—it must be only a medium grade. It must never cause pain. It must never be tight enough to render the distal parts cold. It must not render the skin temperature appreciably lower than that of the opposite limb. It must not induce any paresthesia. And, in the second place, it must not be kept up for more than a few hours at a time. The results obtained in certain cases of acute suppurative inflammation are so remarkable—the disappearance of pain, the feeling of well-being on the part of the patient, the rapid resolution of the inflammation—that there can be no hesitation in stating that, for certain cases at least, the results found are far in advance of any other method. But undoubtedly we have in this matter to proceed with great caution; more investigations are still needed before we can state with precision what conditions of acute inflammation are, and what are not, to be subjected to this treatment, or what exactly are the indications pointing to the employment of passive hyperemia as a therapeutic agent.

We imagine that these will be found associated with the antitoxic, and bactericidal properties of the blood as a whole, that the mere flushing out of the inflamed area is not the main factor, and that more depends upon the leukocytes and their products; if the protective powers of the blood and its corpuscles are markedly lowered, the results of the hyperemia and consequent exudation cannot be so good as when the protective powers are high. (For details of Bier's treatment, see pp. 252 and 638.)

Bier's idea that inflammation is not a process inimical to the organ, and as such to be combated, but the effort on the part of the body to excel or neutralize the injury-working agent, would seem to be confirmed by the epoch-making work of A. E. Wright, who has demonstrated the presence in the blood of what he designates antitropins, precipitins, lysins, and opsonins. It would seem that he has also proved to a demonstration that the opsonins are even of more value than the leukocytes, as the latter are dependent upon the former for their efficiency. That the leukocytes cannot digest or neutralize the bacteria until they have been acted upon, weakened, or rendered vulnerable by the opsonins. These researches would seem to show that, truly, it is not that Bier's method of hyperemia simply flushes out the inflamed area, but that the more active blood-supply brings in through the efferent vessels fresh supplies of leukocytes and antitropins on the one hand, and, on the other hand, causes a rapid removal of the dead bacteria from the field of action.

We cannot too strongly insist that the method is one to be employed with extreme caution: the grade of hyperemia must not exceed a certain limit that is far from being extreme, or be so long continued as materially to lower the vitality of the tissues of the area rendered hyperemic. Otherwise the very opposite results are liable to accrue, namely, growth of the diffused microbes and generalization of the process.

On the whole, to repeat, it is obvious that in cases of acute inflammation the reaction on the part of the organism is in the earlier stages inadequate and, failing excision or operative destruction of the noxa, the rational treatment lies in the direction of promoting a more intense reaction.

(C) Excessive Reaction.—What we have said above indicates that, according to these views, excessive reaction in the case of microbic inflammation is distinctly the exception. We cannot regard those cases as examples of excessive reaction where the results are the production of grave alterations in the part, in the shape either of great tissue destruction or of over-abundant adhesions and cicatricial tissue. Such only indicate that the virus is being antagonized at great cost. There are, indeed, only two conditions which appear to us to come under the category of excessive reaction, namely, (1) where one or other factor in the process is unduly exalted, the others being unduly low, and (2) certain cases of what we may term neurotic and referred inflammation.

As for the first, in cases where the virus is exceptionally virulent, or where, again, the virus is of medium intensity, but through marasmus or other cause the vitality of the tissues in general is greatly lowered, there may be produced a paralytic dilatation of the vessels of an area, with consequent excessive transudation of the fluid from the blood, unaccompanied by leukocytic emigration. It is here that the long-practised linear incisions are of value, in giving free exit to the toxic serum, and in improving the circulation in the blood- and lymph-channels by relieving them of that undue pressure which resulted in almost complete stasis and death of tissue. Or, again, the irritant may set up a local tissue proliferation wholly beyond the local needs. The simplest example of this is seen in exuberant granulations; from these we pass through keloid to conditions perilously near to, in fact, indistinguishable from, certain forms of true tumor formation. As regards the second, we would repeat that reflexly or by central irradiation, through irritation of the nerves in the inflamed area the vessels of areas having the same innervation may in the absence of any direct injury become dilated, and the areas exhibit all the symptoms of an acute inflammation save marked leukocytic migration.

The rapid or great swelling of the tissues around a sprained ankle or knee appear to us to be good examples of this neurotic inflammation. In this latter case we would not say that the swelling is useless. What we would urge is that, once its meaning is recognized, we may proceed not to increase but to allay the hyperemia. So also in the other cases, we are justified in taking such steps as will reduce the excessive development of one or other manifestation.

When under these conditions we conclude that there is excessive hyperemia, there are three main agents that we can employ: The local application of cold, posture, such that as far as possible the blood is drained from the inflamed member, and, thirdly, revulsive agents through which the blood is as far as possible accumulated in other and distant parts of the body.

The only one of these which it is advisable to discuss here is cold and its mode of action.

The application of cold to a part, in the first place, has a distinctly numbing or anesthetic action upon the superficial nerve-endings, and to this extent, provided that the cold be sufficient, its action is grateful and it allays pain. The cold, however, cannot exert a direct influence through any great thickness of tissue; any anesthetic action observed in cases of deep inflammation cannot therefore be direct, and it is doubtful whether it is exerted to any great extent.

In the second place, it causes a pronounced contraction of the superficial vessels and consequent superficial anemia. Here, again, if the inflammation be close to the surface it reduces the hyperemia, and by allowing the exudate to be carried off by the lymphatics at a greater rate than it is formed it reduces the local swelling. If, however, we may judge from experiments on the lower warm-blooded animals, this reduced determination of blood to the part is not of ultimate service. The rabbit's ear infected with pyogenic organisms and subjected to cold, while it shows little swelling and redness, undergoes necrosis, while the other ear, with like inoculation but subjected to warmth, shows an intense inflammatory swelling but undergoes healing. On these grounds cold is of the greatest use in superficial inflammations of non-infective nature.

Thirdly, such superficial cold by acting on the nerve-endings may reflexly influence the other nerve-cells of the same level in the cord and bring about contraction of the vessels innervated from that level. It may thus cause a lessened blood-pressure and blood-supply in the deeper tissues of a part, and if inflammation be present in those deeper tissues, it may lessen the hyperemia there. We would again repeat that, so far as we can see, such lessened hyperemia can only be serviceable in the conditions already indicated where it has previously been excessive.

Here, indeed, we come to the crux of the whole matter. We cannot but bow to the experience of generations of surgeons, that cold applied over certain deep-lying inflammations is not merely grateful to the patient but at the same time serviceable. Admitting this, we have to admit, it seems to us, that in the class of cases in which it is beneficial there is not inadequate but excessive hyperemia. This may be so. The good effects are particularly well seen in acute inflammations of encapsulated organs; in cases of orchitis, for example. After traumatism to a joint it is quite possible that, in addition to its action as a local anesthetic, it may retard or inhibit effusion into the joint by reflexly causing contraction of the blood-vessels, if applied early and under favorable circumstances; that is, in conjunction with rest, posture, and immobilization. It may well be, as suggested to me by my colleague, Dr. G. E. Armstrong, that cold is serviceable when from one or other cause the hyperemia is verging upon stasis. I owe to him the example of the intense inflammatory reaction passing on to gangrene which supervenes when a sufferer from frost-bite of one of the limbs is brought into a warm room and then treated, the gangrene not showing itself when care is taken to keep the limb cool. In the first case, so great is the vascular dilatation and so great the exudation that circulation through the affected part becomes arrested; and, in the second case, the effect of the cold prevents too great a distention of the vessels, so that the circulation is permitted. As we say, where the condition of the part is such that intense hyperemia is verging upon stasis it may well be that the sympathetic or reflex action of external cold, by leading to partial contraction of the vessels and lessened exudation, preserves the circulation through the part and so wards off necrotic changes.

Paradoxically, one of the benefits of the application of cold may be the reactive hyperemia which follows the removal of the cooling agent from the part. There is one other condition which we would tentatively suggest, wherein it may be serviceable; it may rarely happen that it is serviceable to the rest of the organism to give it a rest, to hinder the development of a general toxemia for a time at the expense of continued destructive action at the region of local inflammation.

There are thus, it is true, conditions in which cold applications are serviceable, but I am inclined to hold that these are relatively rare compared with the conditions in which it is of ultimate disadvantage.

On General Systemic Treatment.—If there is anything which has been impressed upon us by the later researches upon inflammation it is that the neutralization of microbic irritants, although in inflammation it occurs at a single focus in the tissues, is not purely a matter of local concern. It is not brought about merely by the local tissue activities, but, save in the very slightest cases of bacterial entry, is a matter in which the organism as a whole is concerned. Space forbids that I enter into this matter at length; into the sites of origin of the migrating leukocytes and the proliferation of the same at a distance; into the debate as to the site of origin of alexins and the protective proteids of the body-fluids and of antitoxic and antibacterial substances in general. I have recently called attention to these subjects at some little length in connection with acute pneumonia and tuberculosis.[33] These are matters more properly discussed in the chapter upon infection. But if this be so, and the organism as a whole has a share in promoting a successful reaction, it follows that in every case of acute inflammation it is of fundamental importance to care for the general health of the patient, being convinced that the healthy activities of the tissues in general are essential to the development by them of increased amounts of these protective substances, as also for the removal of the bacterial toxins which find their way into the blood-stream.

To this end it is well that the tissues be relieved so far as possible of what may be described as the normal metabolic strain. The natural tendency is to reduce muscular activity and to compel the patient to rest, as also to lessen the food taken. These tendencies are to be encouraged; more particularly the diet should be of the blandest and least irritating, the bowels kept open; indeed, saline aperients or mild purgatives are of distinct use. I have already referred (page 187) to the relationship of cryptogenic infections to bacterial absorption from the mucous membranes, and the preventive value of absence of intestinal fermentation.

Whether the inflammation be local or general, toxins are thrown into the body in solution in the body-fluids and must be excreted. Although clinically circulating toxins are intangible, they are infallible in their powers, and it must be remembered that the cumulative action is important, the whole process working in a kind of "vicious circle," so that the greater the severity of the toxin, the less able does the body become to excrete it, and this disproportion becomes greater hour by hour.

The avenues of toxin excretion are many: those over which we have no control, or which we do not intentionally utilize, are the breath, the saliva, and vomitus; those we can utilize are the skin, the kidneys, and the bowel; the more active these agents of excretion are, the more toxin is eliminated, and as a generally accepted, though not a certainly true, corollary, the more diluted the toxin, the less the damage wrought to the organs eliminating it. In view of these beliefs, excretion is to be kept at a high pitch; yet the organs of excretion may be overworked so as to constitute a drain upon the body, and the highest degree of activity short of this is the desirable state.

It is not enough to say that the skin, the kidneys, and the bowel must be rendered active by the use of drugs for that purpose, but the causes of inactivity, if there be such, are to be considered, and as far as possible removed. The mere fact that the patient is in bed, or that his ordinary diet is changed, may be sufficient to induce a torpid condition of the bowel; the kidneys may not excrete freely because the blood-pressure is low or because the heart is weak; the excretion by the skin may be lessened for the same reason. True as it is that tissue waste will be lowered in a patient confined to bed, any inflammation may be enough to counteract this, and the resultant tissue waste be that of normal amount; but, generally speaking, an excess of the secretions of the body is desirable, because the tissues seem at their most active state when the ingestion and output of the body-fluids are both increased. The fact that increased ingestion of fluids dilutes any toxins that may be present in the body is probably of little or no moment.

The tissues are rendered less resistant and less ready to heal by the existence of diseases such as gout and syphilis, and in those who have drunk alcoholic liquors for a long time, or where there has been lately severe disease or debility of any kind. The treatment of these general conditions is essential, and is inextricably bound up with the attempt to obtain as perfect excretion by all channels as is possible. If the local inflammation demands that the general blood-pressure be kept low, rest in bed must be obtained, the diet must be sparing, the fluids taken must be restricted, venesection or purgation used, and such drugs as aconite or antimony may be employed. If the general blood-pressure is too low, and greater stimulation be required, a more generous diet and stimulants, alcoholic and other, are of use. As a general rule, the habit of life that is usual with the patient is to be preserved as far as possible, consistent with the necessities of the case.

The febrile reaction may be so great as to compel treatment, and the most useful method is hydrotherapy, in its various forms, although the existence of a wound often interferes with its use to a great extent. Quinin, salicylate of sodium, alcohol, the coal-tar products, and many other drugs, are used for this purpose.

For the relief of pain it is customary to use analgesics such as opium or belladonna, with local applications of either kind. In all local treatment the possible effect of absorption of a chemical or vegetable poison must always be kept in mind, especially where lesion of the surface exists.

THE TREATMENT OF CHRONIC INFLAMMATION.

It is through no desire to be epigrammatic that one makes the statement that there is no treatment for chronic inflammation; that process consists, as we have seen, of hyperemia, slight exudation, slight diapedesis, and a great tissue proliferation. The last-named process is probably not to be checked by any direct means we can employ; and any mechanical or chemical means we use are likely, *per se*, to increase rather than diminish it. But our mechanical means, directed toward an increase of the rapidity of income and output of the tissues, do more good in this way than harm in the other way. It may thus be said that our treatment of a case of chronic inflammation is not applied so much to the condition, as in spite of it. If fibrosis has taken place we cannot wholly undo it; but by increasing the vitality of the tissues we may check the continuance of the process, and may render the absorption of débris more rapid.

It has to be realized that newly formed fibrous tissue may in some cases undergo absorption. The remarkable diminution in size of syphilitic gummata under potassium iodid can mean nothing else; so also fibroid tubercles scattered over the peritoneum seen at one laparotomy have been found wholly absent at a subsequent laparotomy some months later. This fact affords the suggestion that a mild grade of acute inflammation superposed upon a chronic favors absorption and explains the good effects of induced hyperemia in leading to the removal of adhesions and the restoration of movements in joints.

If a low degree of microbic inflammation be still present, there is an accompanying hyperemia with slowing of the blood-stream; the nutrition of the part, while appearing to be excessive, is often under par, and by the use of various agents we strive to increase its nutrition. Such modes of treatment are as follows: the use of cold for short times at intervals, bringing about an alternation of contraction and dilatation of the blood-vessels; the use of heat more or less continually; the use of electricity, rubbing, handling, and massage of the tissues, to the end that the venous exodus from the part may be more rapid and more thorough; active and passive movement of the part to accomplish the same result by pressure of the contracting muscles; the use of counter-irritation, rubefacients, vesicants, etc., which have this in common, that they probably increase the total amount of blood brought to the part. The use of the seton, now discontinued, had in view the same end.

The result of all these modes of treatment is that the overturn of blood is rendered much greater, the venous return assisted, and the arterial blood permitted to enter more freely. The normal diapedesis of leukocytes tends to the removal of cellular débris, and the circulation in the part is approximated to the normal.

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CHAPTER VI.

SUPPURATION, ABSCESS, AND FISTULA.

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I. SUPPURATION.

Causes and General Considerations.—When the tissues are invaded by certain microörganisms under special conditions suppuration results. It is always preceded by inflammation, and is one of the ultimate manifestations of a struggle between the germs and the resisting powers of the body. It is characterized by the formation of a fluid known as pus, which consists of waste material sacrificed in the contest, together with dead and living germs and their products.

Practically, from a surgical standpoint, there is no suppuration without the presence of microörganisms; but experimentally a spurious pus can be produced by irritating the tissues with various chemical substances, the best known being metallic mercury, turpentine, corrosive sublimate, croton oil, silver nitrate, petroleum, and chlorid of zinc. The toxic products of bacteria dissociated from living germs also produce aseptic pus, as is practically demonstrated in abscesses from sterile catgut.

Suppuration obtained in this way differs from the ordinary variety in that it is strictly limited to the parts injured, and has no tendency to spread or increase in quantity. The pus is often called "chemical" or "aseptic," in contradistinction to that evolved during the growth of living organisms. By some it is even classed as lymph rather than pus.

So much stress has been laid in recent years upon the dependence of suppuration on the mere presence of bacteria that other important factors have largely been lost sight of. As regards the *germs* themselves, for instance, they must be of certain kinds and from sufficiently virulent cultures; their numbers must be great enough to produce an impression upon the tissues; and they must gain entrance in the right way. If they are massed together in pus or blood or other organic material, or accompanied by a foreign body, they are more apt to produce deleterious effects. If they are few in number, scattered, and perhaps suffering from the effect of long-continued dryness, as in dust, suppuration may be slight or absent. It is a phenomenon of great interest, although still involved in obscurity, that when different bacteria are present at the same time (*mixed infection*) their pus-producing powers may be increased or decreased in the most inexplicable and unexpected manner. Germs which under ordinary circumstances are harmless may, for instance, become extremely poisonous, and those which are ordinarily active may become altogether passive.

A lowered *resisting power* of the tissues locally, or of the body in general, is of importance in determining the appearance of suppuration and its extent and character. The *general resistance* may be more or less lowered by such diseases as diabetes, chronic nephritis, scurvy, and certain nervous affections; by starvation, anemia, over-exertion, insomnia, any debilitating sickness, climate, season, poor circulation, inferior or insufficient food, and extremes of heat or cold; by heredity, age and racial peculiarities, and by the excessive use of alcohol, morphin, and other drugs.

Local resistance varies according to the parts concerned, the loosely constructed cellular tissues, for example, being more prone to suppuration than those of firmer build. The amount and character of the vascular supply is also of interest; but perhaps the most important factor is devitalization of the tissues by traumatic or toxic agents. The latter are practically always derived from bacteria and form the key to the whole question of purulent inflammation. Experiments have abundantly shown that pathogenic germs in their growth produce chemical substances known as *toxins*, or *toxalbumins* when they are albuminous in structure. Their local action is to poison the living cells with which they come in contact, thus reducing their vitality and resistance to invasion, and perhaps bringing about their death. They may be found free in the culture-media after removal of the germs by filtration (*ectotoxins*). Or they are confined to the bodies of the bacteria, and are obtained by their disintegration only, when they are called *bacterial proteids* (Buchner) or *endotoxins*. It must be distinctly understood, however, that all the poisonous substances concerned in suppuration do not arise directly from bacteria, but a number are indirect chemical products of decomposition due to the action of bacterial poisons upon the elements of the body. These alkaloids are known as *ptomaïns*, some of the best known being *cadaverin*, *cholin*, and *neurin*.

The general effect of toxins and ptomaïns upon the organism at large is frequently a marked one. Through vascular and lymphatic absorption they act upon the various nerve-centers, and also upon the organs and tissues of the body, producing fever, with its accompanying chills and sweats, nervous and gastro-intestinal disturbances, variations in pulse, etc. They also cause, by their direct action, tissue changes, manifested by cloudy swelling in different portions of the body, such as the kidneys or liver, which changes predispose to secondary or metastatic suppurations caused by the lodgment of bacteria floating in the blood.

The substances which the body produces for the purpose of protecting itself against bacteria and their products (*bacteriolysins*) are of two kinds: *alexins*, which kill the germs, and *antitoxins*, which neutralize their toxic products. They are both probably derived from the disintegration of leukocytes. It is assumed that bacteria are killed both outside the cells in the blood and lymph and within certain cells called *phagocytes*, the latter process being known as *phagocytosis*.

Microörganisms of Suppuration.—Some pus-forming germs, such as certain of the staphylococci and streptococci, habitually give rise to suppuration with ordinarily favorable surroundings, while others, among which are the typhoid bacillus and the pneumococcus, cause suppuration under extraordinary circumstances only. The first are called *obligate* pyogenic bacteria and the second *facultative;* but to draw a sharp line between these arbitrary divisions is impossible owing to the great changes in all bacterial activity under varying conditions.

The principal microörganisms which ordinarily cause purulent inflammation are the *Staphylococcus pyogenes* (aureus and albus), *Streptococcus pyogenes, Micrococcus gonorrhœæ, Bacterium coli commune, Bacterium pyocyaneum, Pneumococcus,* and the *Sarcina tetragena.*

Prominent among those producing suppuration less frequently are the *typhoid bacillus,* the *influenza bacillus,* the *diphtheria bacillus,* the *actinomyces,* various forms of yeast, etc.

Staphylococcus pyogenes (Ogston) (*Micrococcus pyogenes*).—A spherical coccus of somewhat variable size but averaging about .8 μ. When properly stained it can often be seen to be formed of two separate hemispheres. In pus it is generally found in small heaps containing from two to ten members; but it also occurs singly and in pairs, and even occasionally in short chains like a streptococcus, thus rendering diagnosis difficult with the microscope alone. Its cultures are of a yellowish tinge. A paste-like odor is characteristic of "staphylococcic pus."

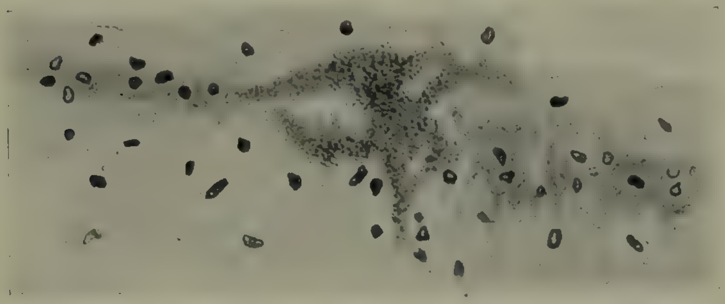


FIG. 42.—STAPHYLOCOCCUS PYOGENES WITHIN THE TISSUES. × 560 (Lehmann and Neumann).

The germs thrive best at a temperature of from 34° C. to 38° C., but are capable of more or less development in any temperature between 6° C. and 43° C. As with other bacteria, the effect of heat depends much upon the amount of moisture present and the particular culture concerned. They will usually withstand, however, a dry temperature of 80° C. for one hour, but moist heat at 70° C. is rapidly fatal. Boiling water kills them instantly, but they seem to resist moist, low temperatures, even repeated freezings and thawings. Prudden kept them alive in ice for sixty-six days. In dried pus they will live from fifty-six to one hundred days (Hägler); and in the human body, especially in osteomyelitic foci, they may remain latent for many years, retaining their virulence and capacity for growth.

Opinions differ so markedly regarding the effects of electricity, of sunlight, the X-ray and other forms of radiant energy that at present little can definitely be asserted on the subject.

Their reaction to chemicals has been extensively studied in laboratory cultures; but the knowledge thus gained is not of such importance to the surgeon as was at first supposed. Dealing as he does with bacteria as they are found in the human organism, the admixture of albuminous bodies is found to inhibit the action of disinfectants so profoundly that the elaborate tables which have been compiled are rendered comparatively useless. It is very difficult to destroy the Staphylococcus pyogenes, as well as many other germs, in infected wounds, without extensive injury to the surrounding tissues. This is readily understood when it is remembered that bichlorid of mercury in so strong a solution as 1 to 1000 will not always kill even a pure culture after an exposure for as great a length of time as five minutes. The pathologic varieties of staphylococci may be distinguished from those which are saprophytic by means of the agglutination test; the former reacting positively to sera obtained through pathologic forms, while the latter remain unaffected (Klopstock and Bockenheimer).

The Staphylococcus pyogenes is found practically everywhere that microörganisms are ordinarily capable of existing, but its presence in numbers in the air, upon the skin, beneath the nails, within the nose and mouth, etc., and upon the various objects usually coming in contact with patients, is of special interest to the operator. It has been estimated that about 10 per cent. of the germs existing in the atmosphere of operating-rooms is of the variety under consideration. They are not numerous, however, in water.

By far the greater number of suppurations are caused by the staphylococcus alone, and it is also present in the majority of mixed infections. It has a special predilection for the skin, penetrating the protecting epithelium through the hair-follicles or through some wound, the sweat-glands being seldom invaded. The osseous system is also frequently attacked.

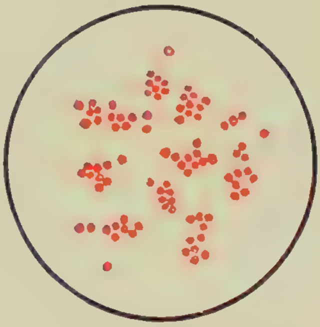


FIG. 43. — STAPHYLOCOCCUS PYOGENES. × 1000.

Two prominent substances are produced during the growth of this micrococcus. The first of these is insoluble confined to the bodies of the bacteria (*bacterial proteid or endotoxin*), and strongly attracts leukocytes from the blood—in other words it is leukotactic. This flow of leukocytes toward a colony of the Staphylococcus pyogenes is very striking and characteristic.

The second substance is soluble and passes out of the cocci into the surrounding tissues and secondarily into the general circulation (*bacterial toxin or ectotoxin*). It is known as *staphylotoxin* and has a profound poisonous action upon all cell-life with which it comes in contact, as well as disturbing the various functions of the body at large—heat-center, circulation, digestion, etc. By its degenerative effect upon distant parts (cloudy swelling), it prepares the way for metastatic infection and may eventually cause amyloid degeneration. It contains *hemolysin* and *leukocydin*, substances which dissolve red and white corpuscles respectively.

Staphylotoxin causes degeneration of leukocytes and fixed tissue-cells. manifested first by cloudy swelling, followed by fragmentation of nuclei and fatty degeneration, and ending in liquefaction of the tissues and the production of pus. This liquefaction is probably due to the liberation of proteolytic enzymes, or ferments, from disintegrating polynuclear leukocytes, rather than to the direct action of bacterial toxins, as was formerly supposed; and to the same cause is due the lack of coagulability in the exuded blood-plasma.

Streptococcus pyogenes (Rosenbach) (*Streptococcus erysipelatis, Streptococcus puerperalis, Streptococcus scarlatinosus*, etc.).—A more or less spherical coccus, varying somewhat in size but averaging about 1 μ, and occasionally approaching the bacilli in form. In pus and in fluid culture-media they are generally found in chains which vary much in length. They also exist singly and in pairs. They thrive best at 37° C., either with or without oxygen, although capable of growing at 12° C., but not above 47° C. Drying is well borne, the germs retaining their vitality and virulence for many weeks, months, or even years, especially if they are dried with pus or blood.

A temperature of 70° C. to 75° C. is required to kill with certainty within one hour cultures suspended in normal salt solution, while two days of a freezing temperature is not fatal (Hartmann).

Streptococci have a very wide distribution in the atmosphere, especially of hospitals, and upon the objects with which we frequently come in contact. They exist upon the surfaces of our bodies, within the mouth, particularly on the tonsils, and to a lesser extent within the nose, vagina, cervix uteri, etc. They are quite often found in the blood and urine, even when no general infection is present.

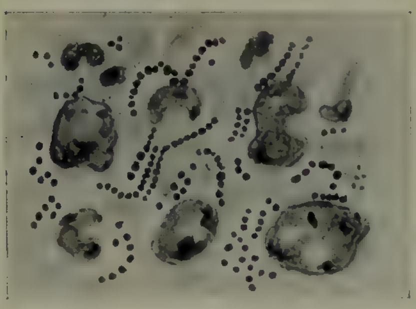


FIG. 44.—STREPTOCOCCUS PYOGENES. × 1000 (Lehmann and Neumann).

Their virulence varies much in different cultures and at different times in the same culture. Cultures which are poisonous to animals are not always so to man, and vice versa. Growth in culture-media rapidly lessens the virulence, while propagation through animals increases it.

Numerous experiments have been made to determine the resistance of streptococci to various antiseptics, but it must not be forgotten that this is a relative matter and varies according to many factors, particularly according to the admixture of albuminous substances. An abbreviated table follows which has reference to pure cultures only. It is based upon the ability to kill in fifteen minutes.

Hydrochloric acid	0.66%
Bichlorid of mercury	0.066%
Sulphate of copper	0.80%
Peroxid of hydrogen	2.86%
Carbolic acid	0.50%
Lysol	0.50%
Pyoktanin	0.22%

When dried on a platinum needle in a thin layer, streptococci are killed in a few seconds to three-fourths of a minute by 1 to 1000 sublimate and 3 per cent. carbolic acid.

When associated with other pathogenic bacteria, the streptococcus sometimes decreases the virulence of the disease, as in lupus, and sometimes increases it, as in other tuberculous lesions. In the latter case it causes so-called hectic or "streptococcus fever," which is often observed in secondary infections of cold abscesses or phthisical lung cavities. The streptococcus and its products seem occasionally to exert a remarkable curative influence over certain new growths, such, for instance, as round-cell sarcoma.

That the Streptococcus pyogenes produces toxins possessing both local and general action is not questioned, but up to the present time comparatively little is accurately known concerning them. Poisonous substances cannot be demonstrated in all cultures, however, even in the most virulent, so that it must be acknowledged that the harmful action of the germ in the production of inflammation, suppuration, and various general symptoms is not yet clearly understood. It is true, however, that its powers are more highly developed within the tissues than in laboratory cultures, and that they consist more in the capacity successfully to resist the bactericidal properties of the body than in the ability to form highly virulent poisons. In spite of assertions to the contrary, no reliable antitoxin has yet been produced.

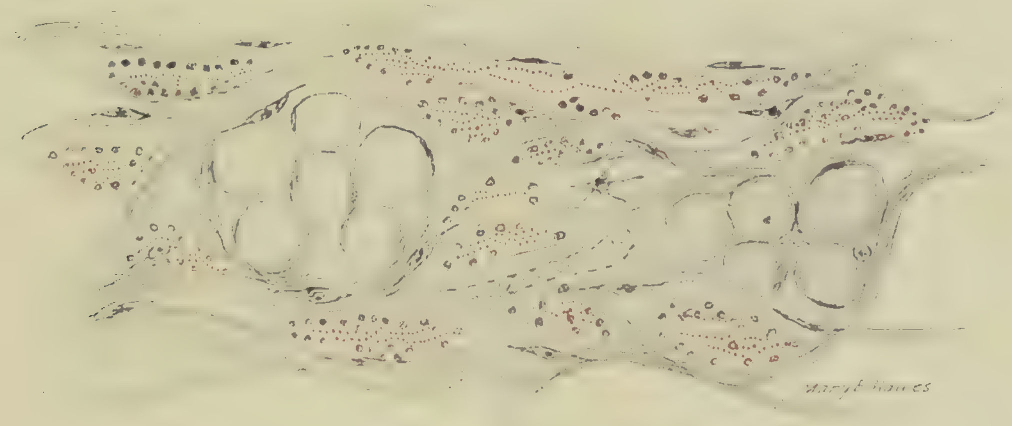


FIG. 45.—STREPTOCOCCI IN LYMPH SPACES.

A prominent feature of the streptococci is the production of *hemolysin*, a non-poisonous substance which has the property of dissolving red blood-corpuscles.

The Streptococcus pyogenes is highly pathogenic and is responsible for a great variety of bodily ailments, such as erysipelas, phlegmon, abscess, lymphangitis, angina follicularis, pyemia, septicemia, enteritis, osteomyelitis, rheumatism, myelitis, etc., etc., and it plays an important rôle in many mixed infections such as occur during the course of diphtheria, scarlet fever, and pulmonary phthisis.

The streptococcus of suppuration and that of erysipelas are now considered identical. They produce one effect or the other according to little understood factors of differing resistance of the individual, size, depth, and location of the point of entrance to the body, varying virulence of cultures, etc.

It has an affinity for the lymph channels and spaces, in which it travels widely and rapidly. It is not obstructed in its progress by leukocytes and fixed tissue-cells, as is the staphylococcus, its leukotactic powers being feeble. The tendency toward liquefaction of tissues and formation of pus is also small, and although its presence is accompanied by violent inflammation, at most an imperfect, watery pus is produced. When marked suppuration appears, it is more apt to be due to a combination with staphylococci, as is well illustrated in phlegmonous erysipelas.

Suppurations in which streptococci exist have a tendency to spread widely; the streptococci preparing the way, as it were, for the staphylococci, after which the former may practically disappear, as happens in many abscesses. Purely staphylococcic suppurations, on the contrary, are generally more limited, being hemmed in by a surrounding wall of leukocytes.

The virulence of the streptococcus is increased by the presence of the bacilli of decomposition, as occurs in some stinking and gangrenous subcutaneous purulent infiltrations.

The streptococcus is the cause of the scarlatinous affections of the skin occasionally appearing in connection with abscesses and infected wounds, and the germ can be detected in the reddened areas.

Although the general symptoms in streptococcus infection are marked, there is nothing absolutely to differentiate them from those arising from the staphylococcus and from other germs. Even the marked up-and-down temperature is not pathognomonic, as has been supposed. The temperature, however, is apt to be high and irregular, with frequent pulse, dyspnea, hebetude, delirium, dry tongue, etc.

Micrococcus gonorrhœæ (Neisser) (*Gonococcus, Diplococcus gonorrhœæ*).—Kidney-shaped cocci, nearly always existing in pairs, with their concave surfaces opposed to each other, and held together by a cementing substance which refuses the ordinary stains. Each pair is from 0.8 μ to 1.6 μ long and 0.6 μ to 0.8 μ broad. The peculiar shape of the gonococcus is extremely characteristic, as is also its prompt decolorization by the Gram method.

It can grow with or without oxygen; best at 36° C., and not at all below 25° C. or above 39° C. It is very difficult to cultivate, as it dies at ordinary temperatures within a few days, or even hours, especially if it is allowed to become dry; hence it is practically never found alive outside the body except on substances freshly soiled by gonorrheal pus. It is never met with in healthy individuals. Its sensitiveness to high temperatures is well shown by the inhibitory action of fevers upon its growth, suppuration often ceasing for the time being. It is easily affected by antiseptics, especially the silver salts.

The gonococcus, although not infectious to animals, is highly so to man, especially to the mucous membrane of the genital tract, and many successful inoculations have been made from pure cultures. It is particularly associated with gonorrhea, endocarditis, metritis, salpingitis, peritonitis, proctitis, cystitis, epididymitis, blenorrhea neonatorum, conjunctivitis, arthritis, abscesses, general sepsis, etc. It is often carried through the lymphatics to the inguinal glands, and sometimes through the blood to the heart, joints, etc.

In pus spontaneously flowing from the urethra the cocci generally appear in clumps within the pus-cells (phagocytosis?) or upon the epithelial cells; but if the secretion has been forcibly squeezed out, this relation is often disturbed and the germs lie in more or less disorder between the cells. Spontaneous rupture of the cells occurs if they contain too many cocci, although as many as 100 or more have been observed without rupture. It has not been demonstrated that the predominance of gonococci either within or without the pus cells has any special bearing upon their virulence.

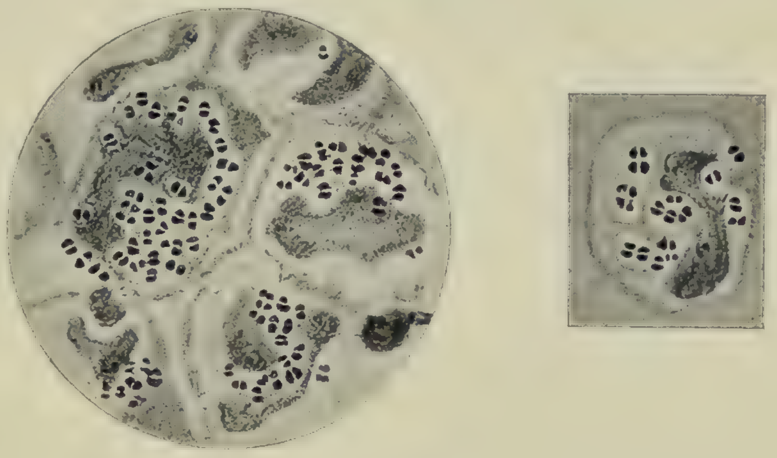


Fig. 46.—Micrococcus Gonorrhœæ. × 1000 (Lehmann and Neumann).

A powerful toxin is formed, which seems to be confined to the bodies of the germs (*endotoxin*). It produces a temporary gonorrhea when injected into the urethra.

Bacterium coli commune (Escherich) (*Bacillus coli communis, Colon bacillus*).—A plump, straight rod with rounded ends, averaging from 1 μ to 5 μ, and supplied with flagella. It possesses active motion and often forms chains. Morphologically, it is identical with the typhoid bacillus.

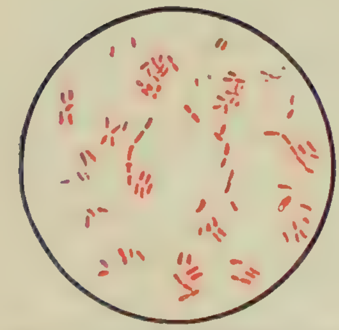


Fig. 47.—Bacterium coli commune. × 500.

It thrives best at 35° C. in the presence of oxygen, although it will grow at a lower temperature and without oxygen. It is not even killed by a temperature of minus 24° C. Growth stops at 45° to 50° C. Foul-smelling gases, such as indol, are commonly produced, together with certain toxins. It can exist in a dry condition for many months. The agglutination test is of diagnostic value.

It is found constantly in abundance in the alimentary canal, especially in the colon, even in the evacuations of the newly born. It occurs also in the mouth and nose, on the skin, under the nails, in the vagina, and widely distributed throughout our surroundings, but mostly where there exists contamination from the bowel contents of man or animals.

The colon bacillus was at first considered harmless; then investigators went to the other extreme and gave it credit for the production of very many diseases. A reaction then set in and it was again regarded as harmless. At the present time numerous infections are placed to its credit. As soon as death takes place, the Bacterium coli has a tendency to wander into all parts of the body through the medium of the blood and lymph-vessels. This peculiarity accounts for the erroneous idea that it was responsible for so many diseases. For this normally harmless germ to become pathogenic its virulence must in some way be increased or the resisting powers of the body lessened, as in ileus; or else it must intrude into parts where it does not normally belong, such as the gall-bladder, urinary tract, etc.

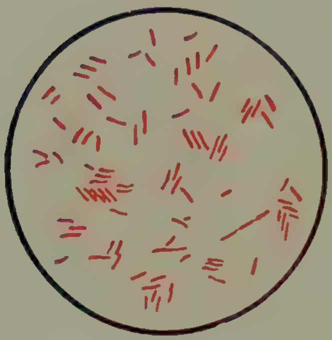


FIG. 48.—BACTERIUM PYOCYANEUM. × 800.

The most characterictic suppurations to which it gives rise are foul abscesses, often containing considerable stinking gas and occurring in the vicinity of the bowel, as in appendicitis. It is often found in the bladder and other parts of the urinary system, sometimes causing severe infections.

Bacterium pyocyaneum (Gessart, Flügge) (*Bacillus pyocyaneus*).—A slender, motile bacillus, 1.4 μ to 6 μ in length, often forming chains, and producing a blue, bluish-green, or green pigment in its growth. It is aerobic, although found in closed abscesses, and grows at ordinary temperatures. It is easily killed by drying. Both *endotoxins* and *ectotoxins* are formed.

It is met with in various situations outside the body, especially in water. In healthy individuals it inhabits the mouth and alimentary tract, and often appears upon the skin and beneath the nails.

Although it sometimes causes suppuration alone, it is generally associated with other pus-forming microörganisms and plays more or less of a secondary rôle, which consists mainly in imparting a bluish or greenish tinge to pus or to the dressings of a suppurating wound.

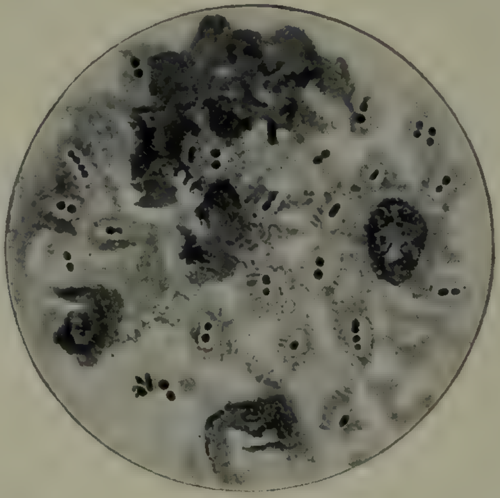


FIG. 49.—PNEUMOCOCCUS. × 1000 (Lehmann and Neumann).

Streptococcus lanceolatus (Gamaleia) (*Pneumococcus, Diplococcus pneumoniæ, Diplococcus lanceolatus capsulatus*, etc.).—A lancet-shaped or round coccus, sometimes the shape of a candle-flame, generally in pairs, often single, and occasionally in chains of from four to six members. When developed within the body it exhibits a distinct capsule. It is closely related to the streptococcus pyogenes in various ways, even if not identical, and a full series of intermediate forms appear between the two.

It grows with or without oxygen; best at 37° C. and scarcely at all at 22° C. It loses its virulence and dies shortly in cultures, and even in the human body this tendency is marked, depending upon the formation of various acids as well as upon other factors.

It is sensitive to light and to desiccation; but when enveloped in albuminous substances, such as sputum, it will live when dried for from fifty-five to one hundred and forty days in diffuse light, although direct sunlight will cause its death in from nine to twelve hours. It is thus evident that the germ can be easily disseminated in dust.

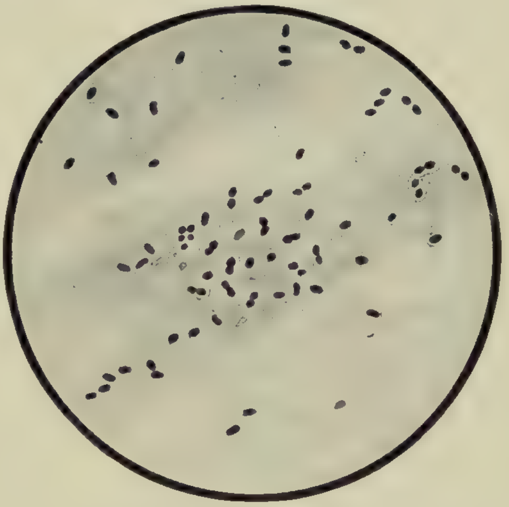


FIG. 50.—DIPLOCOCCUS PNEUMONIÆ. × 1000 (Salinger and Kalteyer).

Comparatively little is known regarding the toxins of the pneumococcus, except that they are apparently small in amount and both soluble (*ectotoxins*) and insoluble (*endotoxins*), the latter being found in the bodies of the bacteria only.

The agglutination-test, although often positive, is uncertain and of little diagnostic value, so that identification must be made by cover-glass preparations, cultures, and inoculation of animals.

It has not been found outside the body very frequently, but it is abundant in the oral and nasal cavities even of healthy individuals, and it occasionally occurs in the lungs. What becomes of it in the alimentary canal when swallowed is yet undemonstrated.

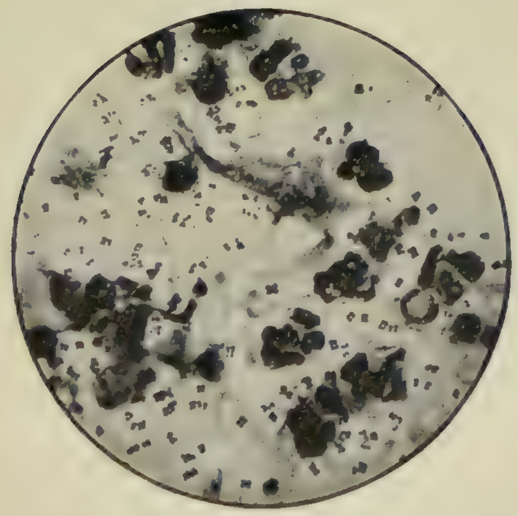


FIG. 51.—MICROCOCCUS TETRAGENUS IN PUS FROM A WHITE MOUSE. × 615 (Heim).

It causes suppuration quite frequently, even dead cultures when injected producing pus; but its most important rôle is played in connection with inflammation of the lungs and serous membranes, such as pneumonia, pleurisy, peritonitis, meningitis, otitis, and arthritis. Osteomyelitis, periarthritis, abscesses of the skin and elsewhere, and general sepsis may also be produced. It is common in mixed infections and is often found in the blood.

Sarcina tetragena (Koch and Gaffky) (*Micrococcus tetragenus*).—A coccus belonging between the sarcinæ and the micrococci and found in pairs or in fours, the latter being particularly the case within the living body. It grows best in the presence of oxygen and at ordinary temperatures.

In healthy individuals it exists within the mouth and alimentary tract, but it is not found outside the body. It is observed in the cavities of tuberculous lungs and in abscesses elsewhere, particularly those about the teeth and jaws. Inflammations in the throat have also been traced to its presence.

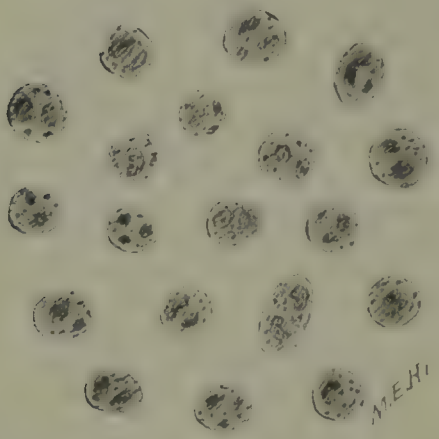


FIG. 52.—FRESH PUS-CELLS, UNSTAINED.

Pus.—Pus is usually a creamy fluid of a yellowish, greenish, or grayish tinge with a specific gravity of about 1030 and containing 80 to 90 per cent. of water. Thick pus is apt to have a green tinge, while thin pus is usually yellow. Its consistency may vary from watery to cheesy; and its color may differ according to many factors—admixture of blood, products of decomposition, the various excretions and secretions of the body, or the color of the germs which exist within it. It may contain flakes of fibrin or mucus. It possesses little if any odor when typical and fresh; but the growth of germs, especially those of decomposition, may render it extremely offensive, as is so often observed in abscesses near the bowel (colon bacillus). The Staphylococcus pyogenes imparts the pasty odor so perceptible when pus is more or less dried on the dressings of a wound.

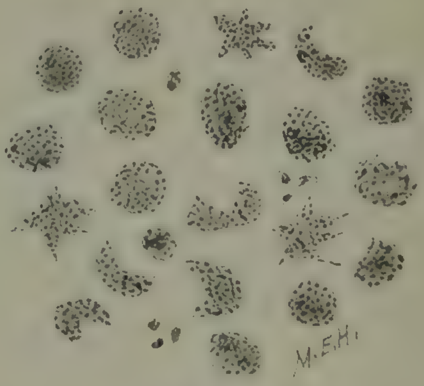


FIG. 53. — DISINTEGRATED PUS-CELLS, UNSTAINED.

The solid elements of pus settle to the bottom when it is allowed to stand in a receptacle, leaving a clear fluid above, which contains bacterial toxins, ptomaïns, and the other soluble products of inflammation. This serum is pale-yellowish in color and is known as *liquor puris* or "pus serum." The precipitate consists principally of polynuclear leukocytes. Proliferated tissue-cells and epithelium are often present, as well as red blood-cells and lymphocytes, which are mononuclear and without granules, together with detritus resulting from cell-degeneration, and dead and living bacteria lying between the corpuscular elements (in gonorrhea the germs are often seen within the leukocytes). A striking characteristic of pus-cells is that they are polynuclear and filled with fine neutrophile, or rarely eosinophile, granules (Plate I, Fig. 3). The nuclei may be brought out more distinctly by employing acetic acid. The cells often possess ameboid movements when the pus is fresh and warm. In older pus the nuclei have undergone fatty degeneration and the cell-bodies may have completely disintegrated (Fig. 53).

Fresh pus is alkaline or faintly acid, but its acidity may be increased on standing. The addition of a strong alkali, such as ammonia, causes the dissolution of the corpuscles and the transformation of the pus into a stringy, gelatinous, or syrupy material resembling thick mucus. This phenomenon is particularly striking in cystitis with ammoniacal decomposition of the urine.

Varieties of Pus.—Under varying conditions pus has received many different names, the majority of which are now but little used.

Laudable pus and *healthy pus* are old terms formerly applied to typical creamy pus arising from free and well-established suppuration. It was supposed to be a favorable indication, although it is now universally admitted that no form of pus is in general desirable.

Ichorous pus, sometimes called *malignant* or *watery,* is thin, of a foul odor, and often irritating and corrosive. When colored with blood it is known as *sanious pus.*

Fibrinous pus, occasionally called *concrete pus,* contains fibrin in flakes or large masses. It is most commonly met with in the pleura, in the cavities of joints, or in the peritoneal cavity. When the fibrinous flakes are few in number, the pus is known as *serous.* In fact, there is a gradual gradation from pure fibrin through regular pus to sero-pus, according to the admixture of leukocytes and fluid.

Muco-pus contains more or less mucus and arises during an inflammation of a mucous membrane.

Tuberculous pus, often designated *scrofulous, caseous,* or *curdy* pus, resembles true pus very closely in appearance, but it is really more in the nature of a fatty emulsion, of tuberculous tissue, and should be regarded as such. The term *caseous* is also applied to ordinary pus which has become thick by inspissation and fatty degeneration.

Gummy pus is not pus, but merely the contents of a broken-down gumma.

According to the color of the microörganisms producing it, there exists *blue* or *green pus* (Bacillus pyocyaneus), *orange pus* (sarcina aurentiaca, hematoidin crystals), *red pus* (bacterium prodigiosum), etc.

In almost all instances where suppuration is once established within the tissues, the pus must evacuate itself or be evacuated before recovery takes place. Exceptionally, however, it undergoes absorption, caseation, or even calcareous transformation, but these changes cannot be depended upon.

Tissue Changes in Suppuration.—Suppuration is practically always preceded by inflammation due to the action of microörganisms. The blood-vessels dilate under the influence of bacterial toxins, and stasis takes place, with exudation of serum and migration of leukocytes, the fixed tissue-cells being in the meantime excited to proliferation. The process, however, does not stop with simple inflammation, but under the injurious stimulation of germ-poisons it becomes grossly exaggerated. By their leukotactic properties the bacteria, especially the Staphylococcus pyogenes, attract from the blood enormous numbers of polynuclear leukocytes, the greatly increased demand for these cells being met by an increased supply from the medullæ of the bones. Chemotaxis may also be exercised by the proliferating tissue-cells. The leukocytes, mainly, together with proliferated fixed tissue-cells and occasionally lymphocytes and endothelial cells from the lymph- and blood-vessels, form a barrier around the invading bacteria, much as a crowd collects about an accident in the street. The process represents an effort of the body at defense—a massing of an army of cells against a microbe enemy—and the facility with which leukocytes can be thrown into the field of action represents to a large extent the success of the defense. Around the Staphylococcus pyogenes, for instance, a restricting wall of cells is produced with comparative ease; but with the Streptococcus pyogenes this cannot be done, the result being in the former case a limited abscess and in the latter a diffuse cellulitis.

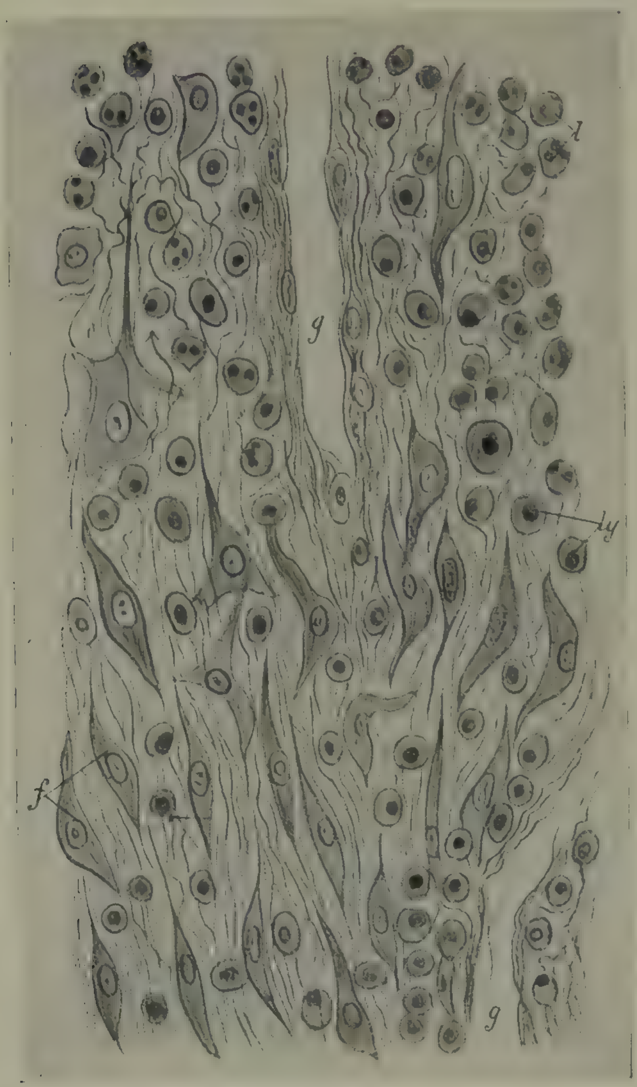


Fig. 54.—Granulation-tissue, seen from the Deeper toward the Upper Surface.

f, Spindle-cells, most abundant in deeper portions, where they are also becoming swollen; *l*, polynuclear leukocytes, most abundant toward outer surface; *ly*, lymphocytes; *g*, capillaries (Ribbert).

The tissues soon become swollen and tense with the abundant serous and corpuscular exudate, thus lessening the blood-supply by pressure. Then begins that peculiar liquefaction of the exudate and the surrounding tissues which characterizes suppuration and results in pus. It is more marked in tissues which have been injured but are still living than in those which are already dead, these latter, which are usually in the center of the inflammatory area, dissolving in the pus at a later stage. It was until recently accepted without question that the process of liquefaction was due to the peptonizing power of certain bacterial products; but there is now excellent reason to suppose that it arises from the action of proteolytic enzymes or ferments which dissolve albuminous substances, and which are set free secondarily by the disintegration of leukocytes. This disintegration is brought about, however, by the action of germ poison (leukolysin).

If the bacteria are stronger than the resisting powers of the tissues, the liquefaction extends and the pus increases in quantity, the wall of protecting cells and the adjacent infiltrated tissues dissolving in the fluid and tumbling into it as do the banks of a rising stream; but new barriers are always being thrown up beyond, until at last they become strong enough or the enemy becomes so weakened, that the invasion is checked. Then begins the process of repair. The tissue-cells form fibroblasts, which finally produce fibrous tissue, and a cicatrix results, the leukocytes playing no part in the regeneration. The waste products in the meantime are removed—the fluids by lymphatic and vascular absorption, and the solids, including bacteria, disintegrated cells, and granular débris, by means of phagocytes. The tissue-growth accompanying active inflammation may be regarded as distinct from that occurring in regeneration, although the two processes often go on side by side. Regeneration begins where inflammation ends, and is a distinct and separate process.

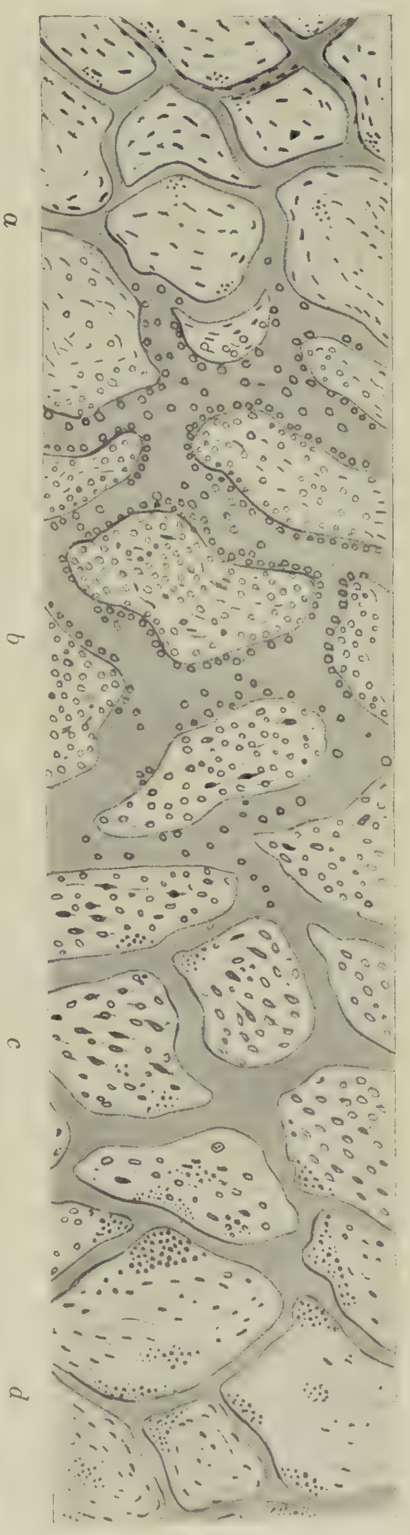


FIG. 55.—SCHEMATIC REPRESENTATION OF CHANGES IN AN INFLAMMATION OF SHORT DURATION, THE VASCULAR SYSTEM BEING REPRESENTED BY THE GRAYISH NETWORK.

a, Is normal tissue. At *b* the capillaries are dilated and emigration of leukocytes is shown. At *c* the formation of new connective-tissue cells is at its height, the leukocytes having almost disappeared. At *d* the process of repair is well advanced, with cicatricial thickening of the tissues, the capillaries having resumed their original small size. Here are also seen groups of lymphocytes surrounding the vessels (Ribbert).

In a general way we may look upon inflammation, and incidentally suppuration, as a beneficial excretory function of the body, always present and busy with small things, but called into exceptional activity by an emergency. Like other functions, it may sometimes result in harm while in the main doing good. It localizes invading bacteria, inhibits their growth, or causes their death. It likewise prevents too rapid absorption of toxins, thus permitting the body to develop a sufficient immunity for its protection. Pus itself hinders the growth and distribution of bacteria and eventually kills them; and when it escapes from the body it carries with it injurious foreign substances, such as bacteria, tissue-débris, etc. This view of inflammation and suppuration might explain why their artificial encouragement by means of poultices and fomentations is often beneficial;

]

and would also lead to the belief that it is not the inflammatory reaction which is really injurious, but the infection which causes it.

Clinical Evidences of Suppuration.—These differ greatly according to the tissues in which the suppuration is situated, its extent and acuteness, and particularly as to whether it is superficial or deep.

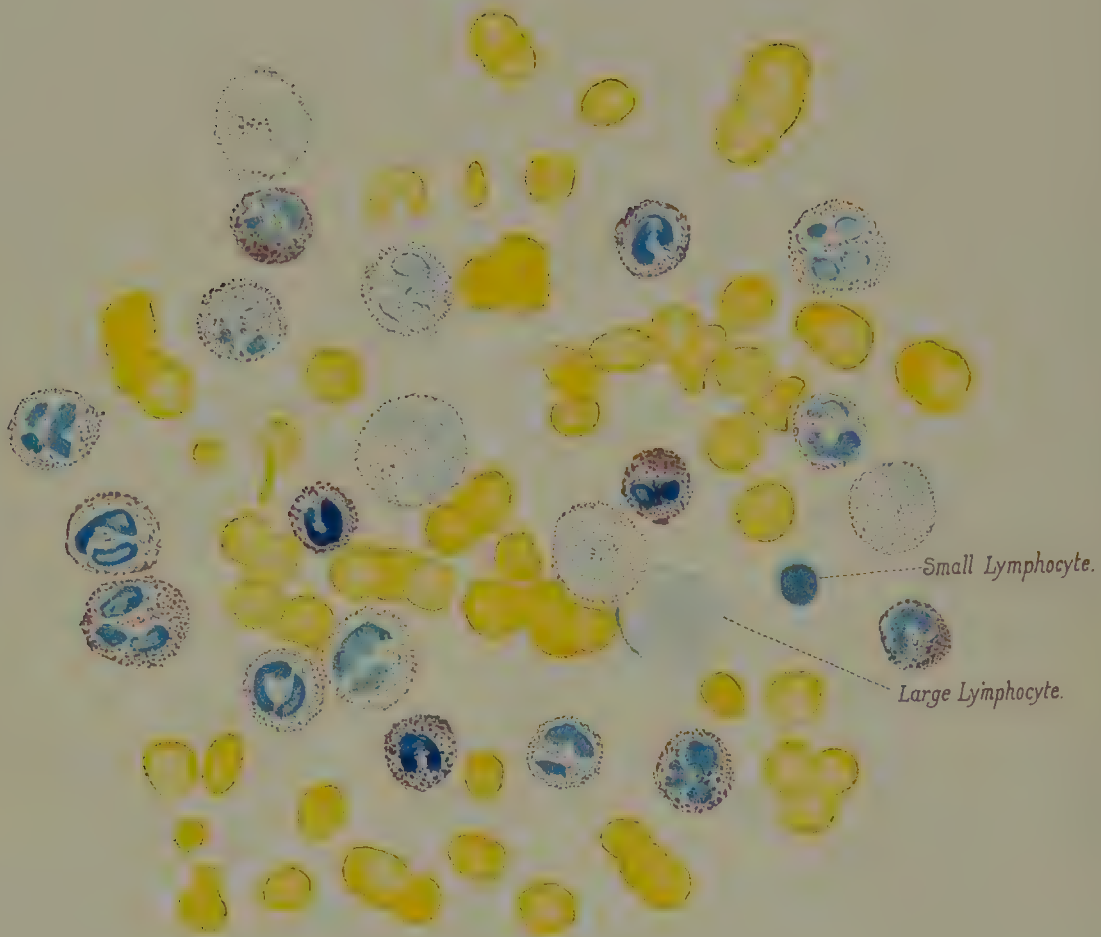
The classic signs of inflammation are heat, redness, pain, and swelling, together with loss of function. All these are more or less intensified as *superficial suppuration* appears. The redness often becomes dusky or mottled as the zone of stasis approaches the surface, and is deepest in the center of the infected area, shading off toward the periphery. The pain increases and becomes throbbing or pulsating in unison with the pulsation of the arteries. Exudation into the tissues makes them tense, swollen, and brawny; the increased pressure, together with direct inflammation of nerves, accounting for the accession of pain. In the middle of this indurated area, at the seat of greatest tenderness, the formation of pus begins ("pointing"), its presence being indicated by softening and "fluctuation," the latter term indicating the sense of the presence of fluid perceived by placing two finger-tips or the finger-tips of two hands together and pressing first with one and then with the other, the second finger or fingers being kept motionless. This should always be done lengthwise of a limb or muscle, because a "*false fluctuation*" can usually be obtained over the muscles in the other direction.

Deep-seated collections of pus are so much more difficult to detect than superficial ones that sometimes diagnosis is impossible. There is often no redness of the skin and no brawniness, although edema and "pitting on pressure" are not uncommon even when the pus is very deep, as in appendicitis, perinephritic abscess, empyema, etc. Rigidity of muscles over a deep-seated abscess is an aid to diagnosis, especially in abdominal suppurations. Pressure symptoms on nerves may furnish excellent evidence of the existence of an abscess, the pain being sometimes referred to distant parts, as in suppuration of the hip-joint with pain in the knee.

The general symptoms of acute suppuration are fever, increased rapidity of pulse, chills or even rigors, sweats, and a feeling of sickness and discomfort. In some suppurations, however, the poison may be so great that the temperature remains normal or becomes even subnormal, as in violent peritonitis. Pus may also exist in the absence of any of the general signs—the pulse or temperature may not be perceptibly elevated, there may be no chills and the patient may feel reasonably well; abscesses of the brain are often of this character. As a rule, however, such infections are unusually mild or extremely well encapsulated, or else the pus has lost its original virulence.

In cases of doubt an *aspirating needle* may be employed, varying in size according to the exigencies of the case. In deep-seated processes this mode of exploration is of the highest service, although great care must be used as regards asepsis. In this way the liver, the pleural cavity, the brain, and other organs and regions equally difficult of access can be explored by repeated punctures with comparative safety. When, however, the needle has to be plunged through an uninfected region such as the

PLATE VI.



Leukocytosis (60,000): Cover-slip Specimen; Ehrlich's Triacid Stain.
The red corpuscles are stained yellow; all the others, except those labelled, are polymorphonuclear neutrophiles (Cabot).

peritoneal cavity, it is well continuously to withdraw the piston of the syringe as the needle is extracted so as to prevent the escape of pus. If leakage is nevertheless suspected, an operation should be done at once, or, better still, an operation should be done without preliminary aspiration.

The length of time during which an acute inflammation has existed is of importance in determining the presence of pus. If two or three days have passed, and the symptoms are increasing or even holding their own, the formation of pus becomes probable; sometimes it may even form in twenty-four to forty-eight hours. This is well illustrated in appendicitis.

The value of *leukocytosis* in the diagnosis of suppuration is not nearly so great as it at first promised to become. It is really but an evidence of the reactive power of the organism against invasion of bacteria, and as such is subject to enormous variations, according to the location and character of the inflammation, the resisting powers of the tissues, etc. Where its help is most needed in diagnosis it often fails; but, nevertheless, it furnishes good corroborative evidence, and should always be taken into consideration in doubtful cases. To be of substantial value, however, the number of leukocytes should be high—approaching 20,000 per cubic millimeter at least, instead of the normal, about 8,000 per cubic millimeter.

Diffuse Cellulitis.—This has been variously termed *phlegmonous infiltration, inflammation,* or *suppuration; purulent infiltration; diffuse phlegmon,* etc.

The term cellulitis is used to designate the more or less extensive, rapidly spreading, generally purulent inflammations of cellular tissues, particularly those which are subcutaneous, although inflammation of the cellular tissues between the muscles, beneath the deep fasciæ, around the bones, in the pelvis, etc., is also included. When adjacent parts, such as tendon-sheaths, muscles, periosteum, etc., are involved, as is frequently the case, for instance, in inflammation spreading up the arm from infection about the fingers, the term cellulitis is often loosely used to cover the entire process. If the inflammation has a tendency to spread rapidly and involve large areas it is called *diffuse cellulitis,* while milder and more circumscribed infections are known as *local cellulitis.* The word *phlegmon* is sometimes employed to cover both abscess and cellulitis, although the adjective *phlegmonous* refers more particularly to spreading than to circumscribed processes.

Causation.—Diffuse cellulitis was formerly thought to be due almost exclusively to the Streptococcus pyogenes, but it is now recognized that the staphylococcus is almost always equally concerned, and may even be the sole offender, at least after suppuration appears. The Streptococcus pyogenes, as it were, prepares the soil by spreading rapidly and widely through the lymph-channels and so damaging the resisting powers of the tissues that the staphylococcus can multiply without hindrance from barriers of leukocytes which would otherwise hold it in check. The resulting pus is due much more to the staphylococcus than to the streptococcus, the latter often disappearing as suppuration progresses.

Other microörganisms, pus-forming or not, are frequently encountered, much more often as a mixed infection than alone. Some of these, such as the bacillus of malignant edema and the colon bacillus, form gases which cause subcutaneous emphysema.

The lowering of tissue-resistance is a factor of paramount importance in the development of diffuse cellulitis. It may arise locally from injury, such as extensive bruises, crushes, or compound fractures; from extravasation of blood; from interference with the blood-supply by vascular lesions; from nutritive disturbances, such as are often seen in spinal injuries; from the presence of irritating discharges—fecal, urinary, etc.; or some general disturbance may be at fault, such as diabetes, chronic nephritis, one of the acute infectious diseases, or some chronic and debilitating illness. Unhygienic surroundings may be contributory.

Erysipelas is a common cause, the streptococcus of this disease and that of suppuration being identical. All that is required is that the germ shall penetrate to and spread within the subcutaneous tissues and be followed or accompanied by the staphylococcus.

A focus of infection can nearly always be discovered, although it is sometimes extremely small, like the prick of a pin, or may have healed before the cellulitis appears, perhaps at a distance from the original wound.

Symptoms.—*The local form of cellulitis* is usually a comparatively mild form of inflammation, often observed about stitches, especially when they have been tied too tight, and in the vicinity of infected wounds, such as those in connection with appendical abscesses. Although the subcutaneous tissues may slough, the process does not spread and recovery is prompt.

Diffuse cellulitis, however, is a much more serious affection, and often ends fatally, from septic thrombosis, pyemia, septicemia, septic intoxication, secondary hemorrhage, etc. The severer forms begin with a chill, followed by a high, irregular, septic temperature, often accompanied by sweats; although when the poisoning is profound the temperature may be normal or even subnormal. The pulse, which at first is merely strong and bounding, is apt to become rapid, and in the later stages weak and irregular, while the nervous system shows the effect of septic intoxication in irritability followed by stupidity and even unconsciousness, thus approaching the typhoid state. There is usually much pain and a sense of tension and burning. The entire aspect of the patient is usually one of extreme illness.

The *local symptoms* vary with the intensity and extent of the disease, the milder forms presenting the appearance of circumscribed inflammation only. In diffuse cellulitis, however, extensive swelling, tenseness and bogginess of the parts soon appear, followed perhaps by fluctuation. If the process is superficial, especially if preceded by erysipelas, redness, soon becoming dusky or even bluish, is an early and prominent feature; but if the inflammation is deep-seated, between the muscles, for instance, the first local signs may consist in swelling only, accompanied perhaps by edema, with pitting on pressure.

Involvement of the lymphatics is frequent and manifests itself by red streaks running from the seat of inflammation to the corresponding lymphatic glands, perhaps in the groin or axilla, which may suppurate in turn.

The disease may progress slowly or even disappear without suppuration, but it often spreads with extreme and alarming rapidity in patients with low resisting powers, especially those suffering from diabetes or Bright's disease. The skin becomes undermined with pus, often over large areas, even an entire extremity or the whole scalp. Subcutaneous sloughs of fascia and other tissues are common. These sloughs are frequently very tenacious, and can be extracted in large masses or in long strings. Gangrene of the skin can result from the action of bacterial poisons and interference with the blood-supply, and when there is much necrosis of tissues even the bones themselves may be exposed or large blood-vessels opened. In such extreme cases, marked cicatricial deformities and contractures sometimes result.

Acute malignant edema, emphysematous gangrene, etc., due to certain gas-forming microörganisms, are considered under the head of gangrene.

Treatment.—Prophylaxis is deserving of the most careful consideration. Thorough antiseptic or aseptic treatment of wounds, combined with drainage when indicated, will prevent most cases of diffuse cellulitis. Wounds, compound fractures, and amputation-stumps which have become septic, should be freely opened, even if they have previously been sutured with care, and inflammatory foci should be subjected to early incision.

After cellulitis has fairly begun, the use of hot or cold moist applications may assist in producing resolution or in alleviating the severity of the disease by favoring capillary circulation. For this purpose the method of Salzwedel is useful. Eight layers of gauze are saturated with 95 per cent. alcohol, applied to the part, and covered with a layer of absorbent cotton 2 to 3 cm. in thickness. Over this is placed oiled silk, to prevent too rapid evaporation, and a compressive bandage. This dressing is left in place twenty-four hours.

If the process continue, numerous and free incisions are strongly indicated; under local anesthesia if the patient's condition be bad, in order to avoid the additional danger of chloroform which may lessen the resistance to sepsis. These incisions should be made as soon as possible and in sufficient numbers and large enough to drain the infected area thoroughly. If done while the tissues are infiltrated with infected serum only, suppuration may be prevented or lessened in amount and destructiveness. As the prime object is drainage, it is much better to employ rubber tubes as far as possible instead of gauze. Moist dressings in the form of hot fomentations are preferable to other kinds because they prevent drying of the discharges and interference with absorption.

It is often of great benefit to place an affected extremity after incision in a continuous bath without any dressing whatever, thus getting the relaxing and soothing effect of the moisture as well as the most perfect condition for continuous drainage. In the treatment by fomentations or baths it should be understood that the use of powerful antiseptics is neither necessary nor desirable, although they are often employed. Strong solutions cause injury to the skin or other tissues, while eczema or general poisoning are not uncommon accompaniments. Particularly should even weak solutions of carbolic acid be avoided, owing to the danger of gangrene resulting. Saturated solutions of boric acid are useful and harmless. If bichlorid of mercury is employed it should not be stronger than from 1 : 10,000 to 1 : 20,000. The part should, of course, be kept at rest, with splints if necessary.

The *general treatment* is of importance and should be stimulating and sustaining. The very free use of alcohol, however, is not so much in vogue as formerly, strychnin having largely taken its place. Quinin is frequently given. The use of antistreptococcic serum, although occasionally encouraging, has been disappointing in this as well as in other affections. If a serum exactly corresponding to the streptococcus concerned could always be obtained, the results might be better, but so exact an adjustment is at present impossible. The serum is injected every few hours as indicated, beneath the skin of the back, sides, or abdomen, in doses of 5 to 10 c.c.

In very severe cases of diffuse cellulitis involving an extremity, *amputation* must at times be considered as a last resort. The condition of the patient, however, must be bad indeed, to justify this procedure, and the surgeon must be reasonably sure that pyemia or septicemia are not too far advanced to permit of recovery. In these discouraging cases Bier particularly recommends his treatment by elastic constriction, claiming remarkable benefit from its use. He also employs it in the milder forms of cellulitis. (See Treatment of Acute Abscess, p. 253.)

If cicatricial deformities or contractures of joints occur, they must be met by appropriate measures. Timely skin-grafting, the application of splints, or the use of passive motion or massage may prevent unfortunate results.

II. ABSCESS.

An *abscess* is a circumscribed collection of pus in a cavity of its own, in contradistinction to *diffuse suppuration,* which is not circumscribed, and to *purulent effusion* or *empyema,* which refers to pus in a pre-formed natural cavity, such as the pleura, pericardium, joints, etc.

Abscesses may be acute or chronic, the latter being nearly always tuberculous and belonging in a class by themselves.

Acute Abscess.—In the center of an abscess are bacteria and perhaps sloughs enveloped in pus which is the result of the conflict of the germs with the tissues. Surrounding the pus is a protecting wall of polynuclear leukocytes, proliferated tissue-cells, and fluid exudate, representing the resisting powers of the body. The innermost layers of this wall show the result of the strife, in that they are crumbling and irregular, partially liquefied in places, and contain many dead and dying cells as well as microörganisms. Further away, however, vigorously resisting and proliferating tissue cells are massed together in great quantities ready to initiate the process of repair as soon as the enemy has been overcome by the leukocytes. Outside this active zone the exudate gradually tapers off into the normal tissues.

As soon as the suppurative process is held in check *fibroblasts,* arising from the fixed tissue-cells, take up the process of repair, which is eventually, after evacuation of the pus, carried on to cicatrization.

The amount of swelling and brawniness of the tissues varies according to the amount of exudate, the extent and intensity of the inflammation, its depth from the surface, the length of time it has existed, and the tissues involved. An acute abscess beneath the epithelium is often a mere purulent blister, while an ischio-rectal abscess may be surrounded by an area of brawny induration as large as the palm of one's hand.

The pus in an unopened abscess is under tension, and hence has a tendency to travel along the lines of least resistance, which are nearly always toward the surface of the body, but may be along deep muscular planes or into cavities or joints. It must be understood, however, that the progress of the suppuration is governed by the liquefaction of the tissues, and that the lack of resistance merely determines the direction. Gravity is not of so much importance in the movements of pus as was formerly supposed, although it plays a part.

As the pus approaches the surface, the skin becomes involved and then thinned and elevated (*pointing*). By palpation, fluid can be detected in the softened area (*fluctuation*), which finally breaks through the necrotic epithelium and the abscess evacuates itself (*bursting*). Some abscesses contain gas, even in large quantities, which puffs out through the incision when the cavity is opened (*gaseous phlegmon*). The gas is nearly always of bacterial origin, usually the colon bacillus, as in appendicitis; although it may come from some neighboring hollow viscus, such as a perforated stomach or intestine in connection with subphrenic abscess; or even from the respiratory tract, as may be seen in collections of pus about the neck or chest.

Causes.—In order that an abscess may occur, three things are necessary—the right microörganisms in sufficient quantity and virulence, their proper implantation within the tissues, and a sufficiently low resisting power, either general or local.

Most abscesses are due to the Staphylococcus pyogenes, although any pus-forming germ, especially the Streptococcus pyogenes or colon bacillus, may be the cause. The bacteria generally gain entrance through a wound, hair-follicle, or sebaceous gland, seldom if ever through the sweat-glands. Other and more unusual ways are through the lymphatics or the blood (*auto-infection*), the absorption taking place from suppurating foci or from the alimentary canal or respiratory tract.

Local cutaneous irritants, especially those which have a tendency to rub the germs into the skin, such as the collar at the back of the neck, the chest-straps worn by soldiers, a truss, etc., are apt to give rise to infections having a strong tendency to recur as long as the cause remains, or even longer. Punctured wounds are particularly dangerous, especially if some foreign body remain in the tissues to which bacteria may cling.

Diagnosis.—In *superficial abscesses* the diagnosis usually presents no difficulties—an inflammatory swelling with redness, local heat, fever, tenderness, throbbing pain, and presenting a softened area near its center in which fluctuation can be obtained on palpation.

In some instances, however, as often happens in inguinal buboes, excessive infiltration of the tissues gives rise to so much browniness that softening appears very late. In such cases it is necessary to judge that pus must be present from the other signs and symptoms, combined with the length of time the inflammation has existed. It is well to remember in this connection that an incision into such an inflamed area, even though no pus is found, is nearly always of benefit and sometimes rapidly curative.

The diagnosis of *deep-seated abscesses* varies in difficulty according to their location. Redness, local heat, and fluctuation are necessarily absent until the surface is approached; but at times a certain amount of browniness and edema of the skin with pitting on pressure may reveal what lies beneath. Rigidity of overlying muscles, especially about the abdomen, is of the utmost importance and is often relied upon alone in suppurations about the appendix. Contractures of muscles, causing bending or ankylosis of joints, are also suggestive, as in flexure of the hip from irritation of the psoas and iliacus in certain cases of appendicitis. As corroborative evidence, leukocytosis, when combined with local and general indications, is of importance, but much less reliance is placed upon it than was formerly the case. Occasionally an abscess-cavity may be detected with the X-ray, especially in the lungs, but the interpretation of such pictures is uncertain and difficult. Unfortunately, some deeply seated abscesses, especially those about the liver and in the brain, may give rise to so few symptoms that a diagnosis can be reached with extreme difficulty only. There may be no chills, no fever, no leukocytosis, and few if any local symptoms—only a feeling of general malaise and loss of flesh and strength. Especially in such cases, as well as in other obscure suppurations, is the aspirating syringe of great use, provided it is employed with due care to prevent infection of adjacent serous cavities. The surgeon should be prepared to operate immediately when pus is discovered in this way. An exploratory incision is often safer and more practical than aspiration, and should sometimes be preferred, especially about the abdomen. In abscesses of the brain or within the bones, an exploratory trephining may be necessary before a conclusion can be reached.

Evidences of pressure upon the nerves or within the brain sometimes help in determining the presence and exact location of purulent foci which would otherwise escape observation.

Prognosis.—This is greatly influenced by the promptness with which pus is evacuated and the thoroughness of subsequent drainage. So important is this that it has become a rule with but very few exceptions that *pus must be removed wherever it may be and as soon as it is discovered.* The exceptions comprise cases—for instance, of appendicitis—where it may seem advisable to let nature build a stronger protecting wall around the abscess before the surgeon interferes; or cases, such as suppurating glands of the groin, in which further softening of infected lymph nodes may be desirable.

Prompt evacuation prevents loss of tissue, poisoning by toxins (sapremia), septicemia, pyemia, and exhaustion from a combination of causes, of which prolonged suffering and lack of sleep are not the least.

Superficial abscesses are, for obvious reasons, less dangerous than those more deeply seated—in the brain, liver, abdominal cavity, bones, etc. Collections of pus in the neighborhood of large vessels should be the cause of particular anxiety on account of the possibility of erosion of the vessel wall and hemorrhage.

Symptoms.—*Superficial abscesses* are preceded by signs of inflammation—redness, swelling, local heat, tenderness, pain of varying intensity, and loss of function. As the abscess develops, these symptoms increase up to the time of free pus formation, when they often subside somewhat, to disappear more or less rapidly when the pus is evacuated. The skin becomes tense and shiny-red from hyperemia, then darker red or mottled from stasis, and finally very dusky or sometimes almost white at the place where pus is pointing and where softening and fluctuation can be detected on palpation. After evacuation the skin wrinkles and the pain disappears, but discoloration of the surface may remain for a long time. Pain is intense or comparatively slight according to the tension of the abscess and inflammation of the nerves, often being of a throbbing or boring character, in unison with the beat of the heart. Pus confined within a space with rigid walls—in a bone, under firm fascia, as in the palm of the hand, within the capsule of the prostate, etc.—gives rise to intense pain, which is at once relieved if the confining wall give way, letting the fluid into the surrounding looser tissues.

Deep-seated abscesses may be lacking in any of the symptoms of abscesses in general, or even at times in all symptoms except loss of flesh and strength. Especially is this true of purulent foci in the liver or brain. Usually there are present local tenderness and pain, pressure symptoms, overlying edema, rigidity of muscles, and ankylosis of neighboring joints, combined with the symptoms of acute suppuration—fever, chills, sweats, loss of appetite, restlessness, etc.

Treatment.—This may be indicated in two words—*incision and drainage.* To be sure, some abscesses, particularly boils, may occasionally be *aborted* by injecting into their center a little pure carbolic acid, but this method is painful, uncertain, and seldom resorted to.

Prior to the formation of pus, the process may often be hastened, if not aborted, and much added to the comfort of the patient by the employment of hot, moist *fomentations* in the shape of poultices, or cloths wrung out of hot water, covered with oiled silk and reinforced by hot-water bags. Whether heat and moisture acts, as insisted upon by Bier, by aiding the beneficial "excretory function" of inflammation is perhaps still open to discussion. An idea is current that strong antiseptic applications are of service, and they are often applied of such a strength as to materially injure the skin. This practice, however, is useless, except in so far as antisepsis may prevent secondary infection when the abscess is finally opened.

Incisions should be large enough to secure and maintain the thorough evacuation of pus; but it is not necessary in all instances to make the great slashing cuts that were formerly considered so necessary, because by the use of rubber tubing a cavity can usually be as thoroughly drained through one or more small openings as through a large one. The incisions must be planned so as to avoid important nerves, vessels, and other structures, and should be made in such a way as to leave the least noticeable scars—in natural folds of the skin, within the hair, inside the mouth rather than on the external cheek, etc. They should be made, as far as possible, at the most dependent portion of the abscess with due regard to the position of the patient so as to secure the aid of gravity in drainage.

An early incision is apt to result in less deformity than a late one, as the loss of tissue and the scar itself will be less. Abscesses opening spontaneously through the skin may leave large, disfiguring, and puckering scars.

Before the days of local and general anesthesia, the opening of a collection of pus with a quick puncturing stroke was a desirable accomplishment, but at the present time it is far less necessary, although it can frequently be used to advantage in superficial abscesses. For this purpose the knife should be guarded by placing the forefinger along the blade in such a way as to limit the amount of the latter entering the tissues. Under anesthesia the method usually adopted is a careful incision with the belly of the knife. If the region is a dangerous one, as soon as the skin is divided blunt dissection, or puncture with a pair of hemostatic forceps, is resorted to, the blades being spread apart as the instrument is withdrawn (Hilton's method). Such a procedure is particularly serviceable in the neck, axilla, popliteal space, etc., thus avoiding injury to the large vessels and nerves of these regions.

Without question there is something to be gained by careful *asepsis* in opening an abscess, by preventing secondary infection with other germs, and yet this gain is not so conspicuous as has often been affirmed. Even though no care in this regard be used, the great majority of abscesses go on to recovery without appreciable difficulty, providing the drainage is adequate and the abscess not tuberculous. In order to diminish the chance of infection of overlying tissues in deep-seated abscesses it is recommended by some to cut down upon the sac and then smear the wound with compound tincture of benzoin or vaselin before evacuating the pus.

It is unnecessary to squeeze out the contents of an abscess; in fact, damage is often done in this way; but it is desirable to extract pieces of loose necrotic tissue if it can be done without injury to surrounding structures. It is not well, however, to scrape the abscess cavity, or in any way injure or break down the cellular barriers which nature has thrown up between the germs and the surrounding tissues. I have seen pyemia result from this practice.

Admitting that *irrigation* is sometimes of advantage, especially in foul-smelling purulent collections and where imperfect drainage exists, in most instances but little, if anything, is to be gained except the mere satisfaction of a general sense of cleanliness; and if strong antiseptics are used, something may be lost by injury to the reparative power of the tissues, to say nothing of the pain and discomfort experienced by the patient. Antiseptics can seldom kill all the germs, but they can destroy many living fibroblasts. If irrigation is employed at all, it is probable that normal salt solution or boric-acid solution is preferable to carbolic acid or corrosive sublimate, in the majority of instances at least.

Drainage should, in most cases, be by means of rubber tubes of sufficient size, rather than by means of gauze. In fact, gauze affords very poor drainage, especially when the pus is at all thick, because the meshes soon become clogged, the gauze dries on the surface, and acts then like a cork in a bottle, pus pouring from the opening as the plug is removed. Through-and-through drainage may be desirable when it can be easily obtained, for instance, the opening of an appendical abscess both from in front and from behind, but it is seldom really necessary. Two tubes placed side by side are often of advantage, especially if it is necessary to irrigate. Instead of tubing, Braatz recommends the use of wire hooks or spiral springs.

Where separate *pockets* exist they must be broken into from the main cavity, and ramifications and burrowings often require slitting up, or at least separate openings at their extremities. A number of smaller openings may be preferable to one larger one for cosmetic reasons.

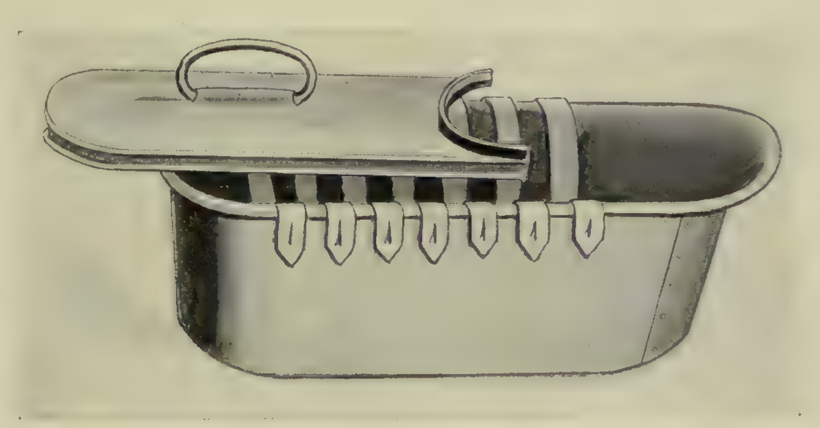


FIG. 56.—BATH FOR INFECTED HAND AND FOREARM (Reichel).

When it is necessary to pass through the free peritoneal or pleural cavity in order to reach a collection of pus, infection may be avoided by carefully *packing off the cavity with gauze*, so as to form a sort of well with the abscess at its bottom. The pus may then be evacuated at once, which is generally preferable, or left from twenty-four to forty-eight hours until protecting adhesions have formed. Careful suturing can sometimes take the place of packing, although even then it is well to reinforce with gauze. Although pus soaks into the gauze employed in this way, it never does serious damage to the cavity beyond, owing to the rapid formation of adhesions. Much of the safety in operations for suppurative appendicitis depends upon gauze packing.

The kind of dressings employed after opening an abscess varies considerably. Where there is much infiltration of the tissues, swelling, and pain, a hot moist dressing is useful, being grateful to the patient and assisting in the process of absorption. Any antiseptic of mild strength may be used, although carbolic acid should be avoided on account of the considerable danger of gangrene. It is not desirable that bichlorid of mercury should be employed stronger than 1 : 15,000 or 1 : 20,000, owing to its damaging effect upon the skin.

Whether dry or moist, the dressings should be loose enough to permit of easy absorption and evaporation of discharges and yet afford sufficient elastic compression to favor collapse of the abscess walls, and in the case of the abdomen, to prevent the viscera from being forced through the opening should the patient vomit or cough. A rather copious dressing of gauze protected by absorbent cotton is generally desirable.

Where the hands or feet are the seat of the suppurative process, they may often be immersed with advantage in *antiseptic baths* without any dressings at all (boric acid, or bichlorid of mercury 1 : 20,000).

Flaxseed poultices are seldom used by surgeons at the present time, although they are probably not so objectionable as has been claimed. Theoretically, they are supposed to favor the growth of germs, but practically abscesses often do remarkably well under their use.

The production of artificial abscesses by the injection of chemicals (turpentine) has been recommended by Fochier and others in the treatment of severe spreading suppurations and general infections, on the principle of increasing leukocytosis and chemotaxis. The method has not received general recognition.

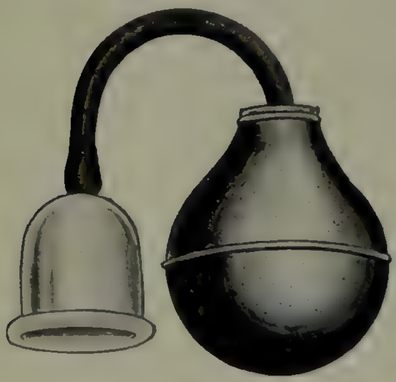


Fig. 57.—Cupping Instrument.

Taking as a basis the modern idea that inflammation is a sort of excretory function of the body designed for its protection, particularly against bacterial invasion, August Bier strongly advocates its stimulation by the production of *artificial venous hyperemia* in cases of acute and chronic inflammation and suppuration. In the past this has been incompletely and empirically accomplished by means of local irritants, poultices, and hot fomentations. Bier, however, proceeds upon a different principle, that of producing passive congestion of the affected tissues. This is done by means of moderate elastic constriction in the case of an extremity; or by means of various forms of apparatus which can be used upon any part of the body and which work, like the old-fashioned "cup," by the formation of a vacuum. The latter method has an additional advantage, according to Bier, in that pus and sloughs may thus be sucked out of a previously opened abscess without the dangers incident to evacuation by squeezing. In practice, glass cups or chambers are employed, fashioned to conform to various sized abscesses situated in different portions of the body, the air being moderately exhausted by a rubber bulb or an air-pump. A hand or a foot may sometimes be placed to advantage in a sort of vacuum-box, the entrance to which is surrounded by a rubber cloth which is bandaged about the limb before pumping out the contained air. By a modification of this apparatus, contractured joints may be straightened by atmospheric pressure.

Admitting that this principle of treatment is of value, although it is as yet far from being universally accepted, it must be clearly appreciated that much depends upon its correct application, the details of which should be carefully studied in Bier's treatise.

Too much care cannot be used in the application of constriction, especially in cases of severe inflammation where the circulation is already poor, for fear of endangering the vitality of the limb. A thin rubber bandage should be employed (Martin's bandage) and wound just tightly enough about the extremity, well above the inflammatory focus, to produce venous congestion without arterial obstruction. It should be placed above the elbow when the hand is involved, and above the knee in case the foot is the seat of the difficulty. In acute inflammations, considerable redness and swelling immediately occur, extending often up to the constricting band. Little if any pain or discomfort should result; in fact, the pain should be quickly relieved. In chronic cases swelling and redness are not produced. Suppuration is generally increased at first, and then becomes lessened and rapidly disappears, along with edema and redness—in other words, the infective agent is inhibited in its growth and then destroyed.

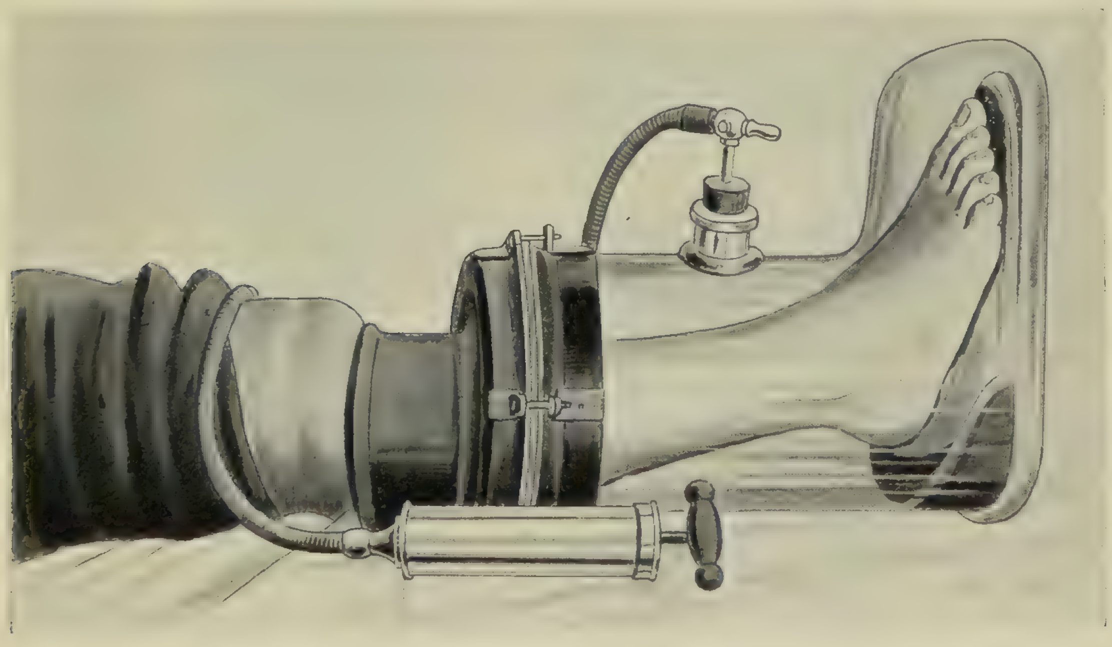


FIG 58.—APPARATUS FOR HYPEREMIA.

Under watchful supervision such a bandage may be left in place for many hours. Acute cases demand at least ten hours daily, and at times as much as twenty-two hours, in order to obtain good results; although, on account of discomfort to the patient, pauses in the treatment may occasionally be necessary.

The vacuum-method cannot, as a general rule, be used continuously, one sitting a day being as much as can be borne with comfort. During this time the cup may be applied for say three minutes and then removed for five minutes during the course of perhaps three-quarters of an hour.

As suppuration ceases, and the discharge becomes more watery, the treatments may be given every second and then every third day, and so on until recovery is attained.

Unless the greatest care is used in regulating the amount of air withdrawn and the length of the sittings, the vacuum-method of handling acute inflammation is more or less painful, so much so that it has been discarded by some.

At the present time it can be said that the strongest indications for the Bier treatment are to be found in cases of chronic inflammation and suppuration, particularly when they are tuberculous in nature, and in these many encouraging results have been obtained.

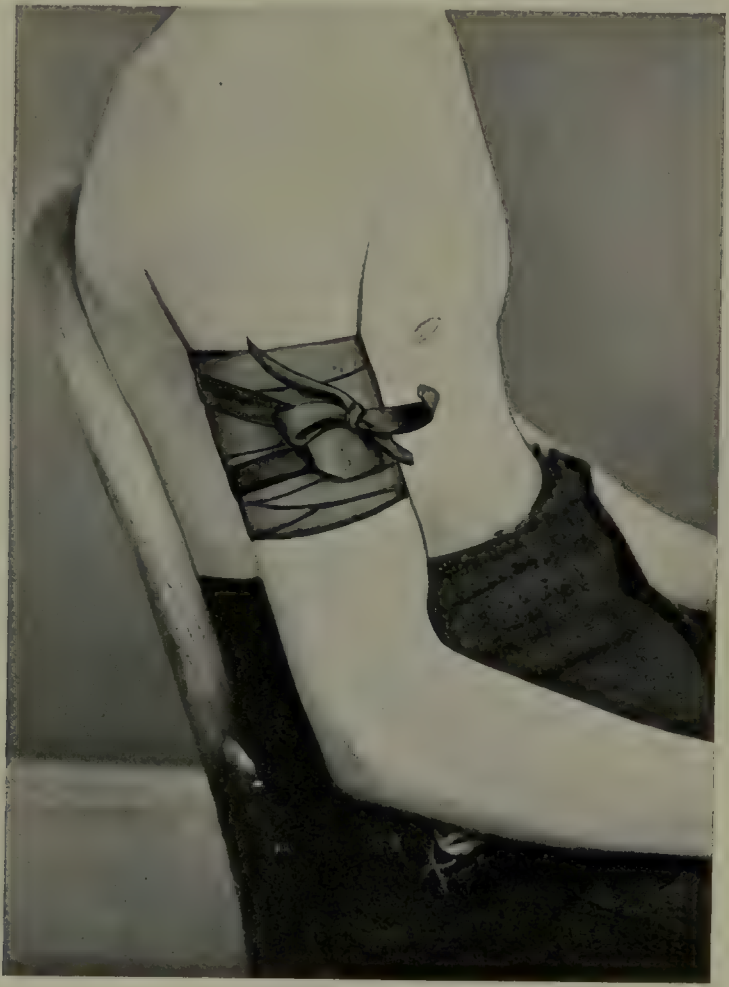


FIG. 59.—MARTIN'S ELASTIC BANDAGE APPLIED.

Sergent's suggestion relating to the internal administration of beer-yeast or a preparation obtained by macerating sterile yeast in water is still on trial. Preparations of desiccated yeast may be obtained for this purpose also. The method is supposed to influence abscesses of the skin only, as in furunculosis. Fresh brewers' yeast is usually employed in doses of ʒj to ʒij in water just before or during meals. Diarrhea sometimes results, even when the yeast is quite fresh. The internal administration of drugs, such as the sulphid of calcium, which was at one time extensively used, is almost universally acknowledged to be of but little service; although proper attention to stimulation, nutrition, and general hygiene are often of considerable moment.

Varieties of Acute Abscesses.—Some of the names are obsolete, and others sufficiently describe themselves.

Circumscribed abscess.

Encysted abscess, one occupying a portion of a serous cavity.

Diffuse abscess, a more or less disseminated collection of pus.

Superficial abscess, one above the deep fascia.

Deep or subfascial abscess, one beneath the deep fascia.

Internal or visceral abscess.

Congestive, gravitating, wandering or *hypostatic abscess* refers to pus collections which work their way from one point to another, gravity having less to do with the progression than do the lines of lesser resistance in the tissues.

Critical or *consecutive abscesses* are those which seem to be the culminating point of some acute disease. In most instances, however, the symptoms of suppuration are mistaken in reality for the supposed disease, or else the formation of pus is a mere coincidence.

Milk abscess occurs in the breast during lactation.

Sympathetic abscess arises in connection with some other focus of infection, generally through the lymphatics—for instance, an axillary abscess from an infected finger, or a bubo from a sore upon the penis.

Pyemic, metastatic, or *embolic abscesses* arise from infected emboli carried through the blood. They are usually multiple and occur in various portions of the body at the same time.

Thecal abscesses occur in connection with the tendon-sheaths.

Diathetic abscesses arise apparently in connection with some diathesis.

A *tympanitic, gaseous,* or *emphysematous abscess* or *phlegmon* contains gas or air, the former arising from the growth of bacteria, usually the colon bacillus, and the latter from connection with a perforated stomach, bowel, trachea, or bronchus. Certain subphrenic and appendical abscesses form good illustrations.

Fecal or *stercoraceous abscesses* contain fecal matter. This is not always to be determined by the odor, however, because the growth of the colon bacillus and other bacteria often so taints a collection of pus as to cause it to be mistaken for fecal material, particularly if gauze drainage is employed.

Follicular abscesses are found in connection with follicles, as in the tonsils.

Hematic abscess is caused by infection of a blood-clot in the tissues. This is uncommon unless there is some connection with the atmosphere.

Marginal abscess is so called because it appears at the margin of the anus.

Ossifluent applies to abscesses in connection with diseased bone.

A *tropical abscess* is an abscess of the liver deriving its name from the fact that it is most common in the tropics, although occurring elsewhere.

Urinary abscess is found in connection with decomposing urine which has found its way into the tissues, for instance, in rupture of the urethra.

A *verminous abscess* contains some form of intestinal worm, more often the round worm, and has usually a connection with the bowel.

Acute Abscesses in Different Regions.—**Furuncles or Boils.**—These are small, well-circumscribed abscesses of the entire thickness of the skin and extending more or less into the subcutaneous cellular tissues. They usually arise from inoculation of a hair-follicle, or possibly a sebaceous gland, with the Staphylococcus pyogenes; although other micro-organisms may be at fault, and the infection may take place through some small abrasion without the involvement of a gland at all. From the action of bacterial toxins and the arrest of nutrition by tension of the infiltration in the dense cutaneous tissues, a central slough or "core" generally results, which contains the hair-follicle and sebaceous gland, and which is finally loosened and cast off by surrounding suppuration, leaving a cavity which heals by granulation. If the entire skin is involved a scar results.

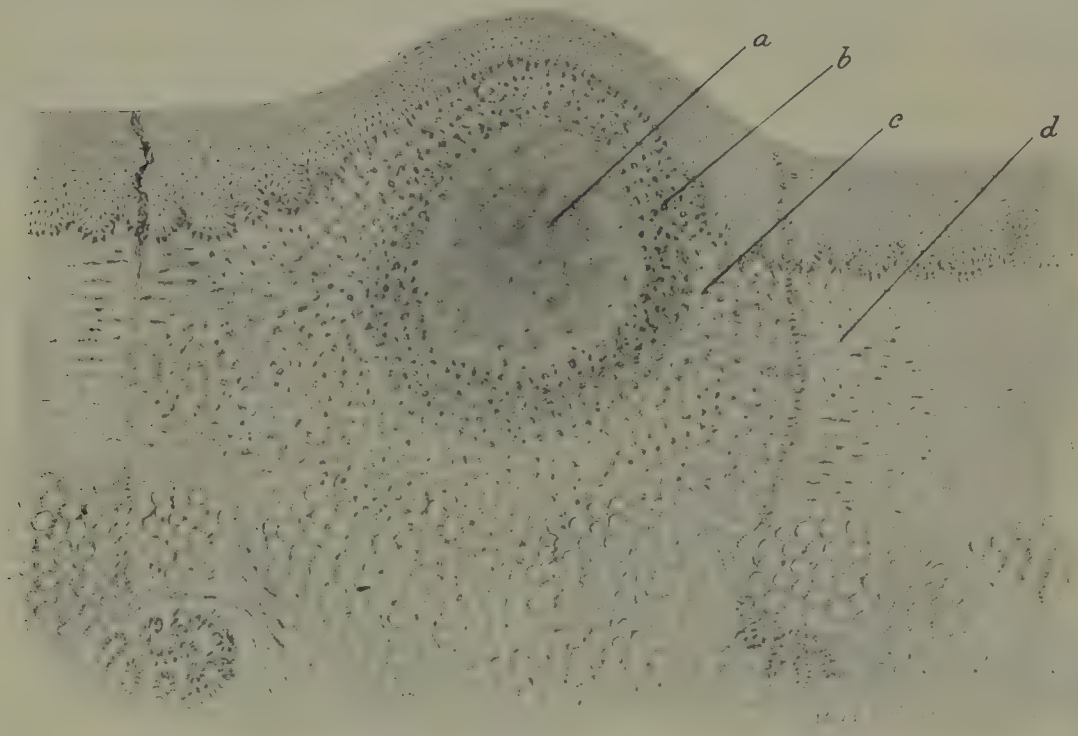


Fig. 60.—Formation of a Furuncle.

Showing, *a*, central core of pus; *b*, surrounding zone of densely crowded leukocytes; *c*, zone of less crowded leukocytes, and *d*, outer zone of fibroblasts. The epidermis is lifted and thinned by the pressure of the infiltration in the connective tissue below it (diagrammatic).

Anything which lowers the local or general resisting power predisposes to the development of boils, especially diabetes, chronic nephritis, insufficient or improper food, anemia, and the debilitating effects of typhoid and other fevers. Local irritations of the skin, particularly those in which bacteria may be rubbed in, as on the back of the neck by the collar, or about the nates in rowing, are of importance in causing these local suppurations, as is also uncleanliness or even too much bathing.

A furuncle begins like an ordinary pimple, except that the irritation, itching, and burning are usually greater. In the course of several days it develops into a hard, dusky red swelling with a superficial pustule at its apex which may burst, leaving a small crust. There is much tenderness and pulsating pain, and constitutional reaction is often marked. Softening appears as suppuration takes place and the necrotic core may be detected as a small black or white spot. If let alone the boil will evacuate itself in the course of about a week through a ragged opening in the necrotic skin. It is seldom that extensive cellulitis or serious inflammation of adjacent lymph nodes results.

An unusually deep involvement of the subcutaneous tissue is called a *carbuncular boil.* A *blind boil* is one which does not suppurate, although absorption is often long delayed. When a number of boils appear at one time, or a succession of boils extend over a length of time, the process is known as *furunculosis.* It may be general over the body or local, and is sometimes epidemic, especially in the army or in institutions of various kinds. Small boils occurring in numbers in the beard are called *sycosis* and a boil upon the margin of the eyelid a *sty.*

Although furuncles may appear at almost any place about the body, they are most often found upon the neck, back, nates, hands, or face. They are more common in youth than in age, although occurring at all times of life.

Treatment.—In those who are subject to boils, prophylaxis is of importance. This means that exercise, proper diet, and correct living must be insisted upon, together with cleanliness of the skin without too much bathing. With the exception of tonics there is no medicine which can be relied upon, although many have been suggested, including yeast (see p. 254), calcium sulphid (grain $\frac{1}{6}$ three times daily), arsenic, etc.

In the very early stages a boil may sometimes be *aborted* by covering it with collodion; or by extracting the central hair, opening the superficial pustule, and inserting a little 95 per cent. carbolic acid on a sharpened stick. Later in the process a drop or two of 3 per cent. carbolic acid or some other antiseptic, such as 15 minims of methylene-blue (1 : 500), may be injected into the center of the infiltration; or electrolysis or the actual cautery may be employed. These methods of abortion, however, are painful and unreliable. The accepted method of treatment is to apply hot moist fomentations until the boil is mature or "ripe," then open it as soon as pus has begun to form, afterward dressing it with a little cotton and collodion or with warm moist antiseptic dressings according to the size and amount of inflammation and infiltration. In incising a boil an anesthetic is often unnecessary; but when it is required, local anesthesia is preferable to general, although nitrous oxid gas or somnoform are at times of great service. The injection of Schleich's solution or a weak solution of cocain is far preferable to the local use of chlorid of ethyl, on account of the acute pain produced in an inflamed area at the moment of freezing.

Carbuncles.—A carbuncle is a circumscribed inflammation of the subcutaneous connective tissue involving and perforating the skin, usually in several places, and accompanied by suppuration and sloughing of the tissues. It differs from a boil principally in that it is more extensive and spends its force more deeply and profoundly. Like a boil, however, it is generally due to the Staphylococcus pyogenes, which enters through a hair-follicle or an abrasion, rarely through the blood or lymphatics. A small superficial inflamed spot first appears, which soon spreads deeply and widely, producing an extensive, indurated, perhaps boggy infiltration, more or less flat, elevated and circular in shape, and of a dusky red, purplish, or coppery color. The area involved is often several inches in diameter, occupying, for instance, the entire posterior portion of the neck, and extending possibly onto the scalp and the skin of the back.

Small pustules soon appear upon the surface which break and reveal the mouths of openings which lead through the skin to the sloughing tissues beneath. These multiple openings are characteristic of a carbuncle. They represent the paths of least resistance through the skin along the columnæ adiposæ, by way of which the pus reaches the surface.

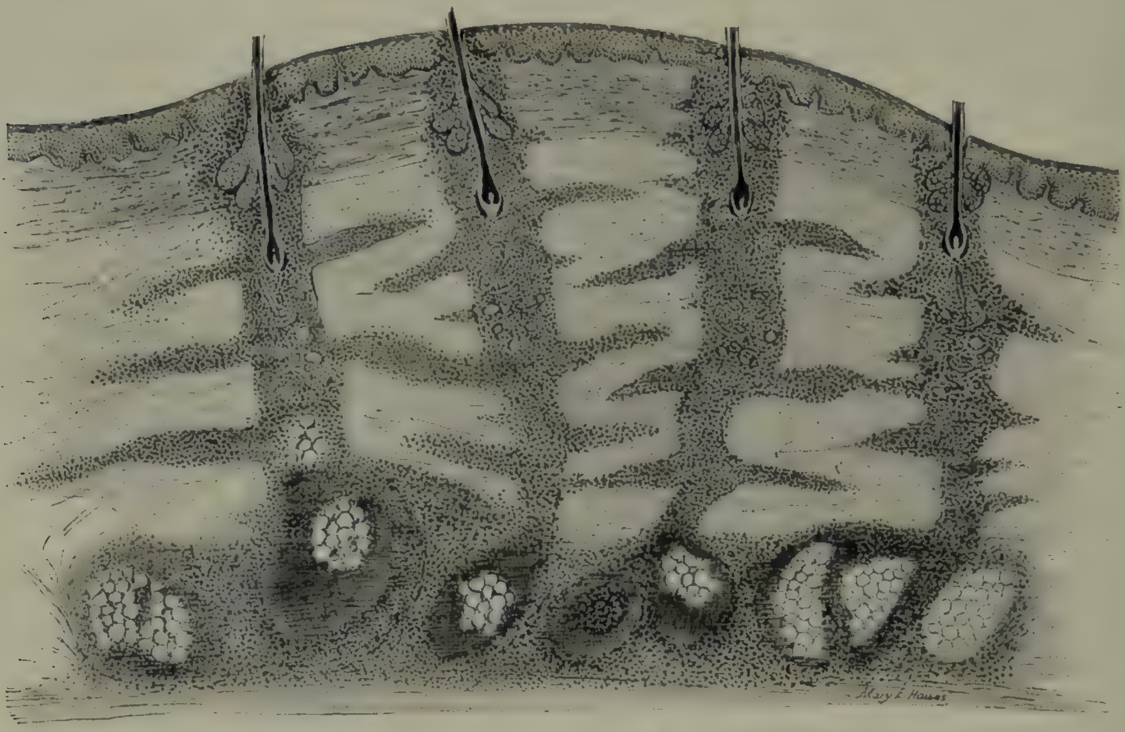


FIG. 61.—SECTION OF A CARBUNCLE OF THE BACK, SHOWING INFILTRATION OF THE ADIPOSE LAYER OF THE CUTIS VERA AND EXTENSION TOWARD THE SURFACE THROUGH THE COLUMNÆ ADIPOSÆ.

Portions of skin of greater or less extent may become gangrenous, the tissues melting away into large ulcers having undermined borders and lined with sloughs. In this way muscles may be exposed and even destroyed.

Carbuncles are particularly apt to occur in those suffering from diabetes, Bright's disease, or other debilitating troubles, and the appearance of one should always be an indication to examine the urine for sugar and albumin. They occur most frequently on the nape of the neck and the back, the thickness and anatomic peculiarities of the skin and subjacent tissues of this region being largely responsible.

Carbuncle of the upper lip is peculiarly dangerous, the majority of cases being fatal, owing to the likelihood of septic phlebitis involving the facial vein and through it the ophthalmic leading to the cavernous sinus.

The *general symptoms,* beginning with a chill, are almost always profound, owing to the influence of marked sepsis upon a constitution already debilitated from other causes; the temperature, however, may not be high. Weakness, apathy, and even coma are frequently, although not always seen. In exceptional cases, where the disease is mild or the resisting powers unusually good, the constitutional effects may be remarkably slight.

Treatment.—A carbuncle can seldom be aborted, although injections of carbolic acid into and around it have been advised. The most effective procedure, especially in severe cases with marked sepsis, is to excise the entire lesion into sound tissues, followed immediately by skin-grafting according to Thiersch; although a crucial incision, or multiple incisions combined with extirpation of sloughs with a sharp spoon and scissors and disinfection with pure carbolic acid, and later on skin-grafting if necessary, gives satisfactory results in many cases. Local or general anesthesia can be employed. The after-treatment should consist in the use of hot antiseptic fomentations and frequent cleansing irrigations.

General treatment is of importance and should be stimulating and sustaining, due consideration being given to the presence of sugar in the urine. (See chapter on Surgery of the Skin and its Appendages.)

Abscess of the Brain.—Abscess of the brain may arise from micro-organisms carried through the blood from some focus of infection elsewhere, for instance, in the heart or in the lungs; but the most usual cause is suppurative inflammation of the middle ear. Fracture of the skull, compound or otherwise, may give rise to the abscess either at the time, or weeks, months, or even years subsequently.

The collection of pus may be extra-dural, between the bone and the dura; sub-dural, between the dura and the brain; or within the brain substance itself—cerebral or cerebellar. It is usually single, but may be multiple, and sometimes reaches enormous dimensions, even occupying an entire lobe.

The most striking feature among the *symptoms* is the usual absence of fever, except in the extra-dural form, the temperature being often even subnormal. Hence, the diagnosis must be based on the history combined with general and local pressure symptoms, such as dullness of mind, coma, change of character, slow pulse and respiration becoming Cheyne-Stokes or stertorous, choked discs, vomiting and vertigo, paralysis, aphasia, headache, leukocytosis, etc.

The only *treatment* is evacuation of the pus through a trephine opening.

Von Bezold's Abscess sometimes occurs rather late in the course of a mastoiditis, from perforation of the inner wall of the process at its tip, either through a natural opening or a necrotic area of bone. The infective material escapes into the digastric fossa, and from there may burrow extensively among the tissues of the lateral aspect of the neck. It gives rise to a brawny painful swelling involving the glands and finally the skin itself, which becomes red and thickened. Coincident with the cervical swelling, which takes place rapidly, the pain in the mastoid and the oral discharge are apt to lessen considerably. In some respects the affection resembles sinus-thrombosis with involvement of the internal jugular; but the rapidity and extent of the swelling, the absence of the extreme variations of a pyemic temperature, etc., are distinguishing characteristics.

Treatment should consist in incision and drainage, with a free opening near the apex of the mastoid, and removal of its tip when considerable necrosis exists.

Abscess of the Orbit.—Abscess in the cellular tissue of the orbit may arise from various causes, the most prominent being periostitis, facial erysipelas, inflammations about the teeth of the upper jaw, pyemia, and suppurative inflammation of the accessory sinuses of the nose and base of the skull. It sometimes follows meningitis or the acute exanthematous fevers.

In marked cases the constitutional symptoms are pronounced and the local signs striking. The eyelids are apt to be enormously swollen and discolored with edema of the conjunctiva (chemosis). The eyeball is protruded and turned slightly outward and the sight soon becomes defective. Panophthalmitis may result. Pain, tenderness, and headache are prominent features of the disease and meningitis may supervene.

In the early stages local depletion is often used, by means of leeches and hot fomentations, although their utility is questionable. Pus should be evacuated as soon as possible by means of an incision through the conjunctiva near the orbital wall.

The occurrence of suppuration within the eye itself may call for evacuation and subsequent enucleation.

Abscess or Empyema of the Antrum of Highmore.—Abscess of the antrum is usually due to inflammatory lesions about the jaws, teeth, or within the nose. It is especially prevalent during epidemics of influenza. Occasionally an aberrant tooth or a piece of carious bone is found loose within the cavity. When the antrum fills with pus, which is often offensive, it has a tendency to flow into the nose, especially if the head is lowered and turned to the opposite side. If, however, the opening into the nasal fossa be closed by inflammatory swelling, the tension within the cavity may become great enough to cause enlargement of the cheek, protrusion of the eye, and even crepitation of the thin and expanded bone. Chills, pain, fever, and tenderness are common symptoms during the acute stage. A shadow on the diseased side, as shown by transillumination by an electric light in the mouth, is an important diagnostic sign, as are also swelling and edema of the overlying tissues.

The most effective *treatment* consists in thorough and prolonged drainage combined with frequent irrigation. This is obtained by extracting a diseased tooth and perforating the alveolus at its root; by making an opening through the wall of the antrum just above the alveolar process with a trephine or chisel; or by perforating the cavity through the nose in the inferior meatus. A combination of the two last named methods is particularly effective and often used in bad cases.

Alveolar Abscess (Commonly called "Gum-boil").—This arises within an alveolus from infection through a diseased tooth or from the margin of the gum. It is in reality a periostitis or periodontitis, followed by ostitis as the process advances, ending in the formation of a cavity within the bone. Resolution may occur in the early stages, but usually the pus finally burrows through the alveolar plate and forms a fluctuating swelling beneath the gum. Most cases are comparatively mild, but occasionally violent cellulitis or extensive periostitis is set up, resulting in septic poisoning and perhaps extensive loss of bone. Perforation into the antrum of Highmore with resulting empyema is not uncommon, and if the abscess opens externally upon the cheek, usually upon the margin of the lower jaw, an unsightly puckered scar or perhaps a sinus will remain.

The *symptoms* are usually trivial, but they may be extremely severe. There is generally swelling of the cheek, which may be enormous, and the jaws can become firmly locked so that chewing is impossible. The pain is frequently intense and throbbing. The affected tooth is loosened and seems lengthened, and it actually is pushed somewhat from its socket by the effusion beneath.

The *treatment* consists in the use of hot applications and morphin to relieve pain, together with early opening of the abscess. It is sometimes necessary to trephine the alveolar plate in order to obtain better drainage. If the tooth is worthless it should be extracted, otherwise later on it can be disinfected and filled.

In order to avoid deformity, abscesses involving the cheek should be opened from the inside, even though they are upon the point of opening externally. Dead bone must be carefully removed. Resulting depressed scars may be excised or loosened with a tenotome and filled out with paraffin.

Abscesses of the Larynx are always accompanied by edema, which may endanger life through interference with respiration. They most often develop upon the oral surface of the epiglottis, but may occupy the aryepiglottic folds or even the true vocal chords. When not visible from the mouth, they can be detected with the laryngoscope or the finger.

The *symptoms* of most importance necessarily center about the edema, which may develop with startling rapidity, causing death from suffocation. Pain and difficulty in deglutition are also present, as well as the usual constitutional disturbances accompanying suppuration.

The *treatment* consists in early evacuation of pus. Edema may be combated by the rapid swallowing of pellets of ice, together with cold applications externally. Scarification of the swollen mucosa must at times be done. Tracheotomy, rather than intubation, is indicated in bad cases, even as a prophylactic measure where stenosis has not yet occurred.

Deep Abscesses of the Neck.—These arise in the majority of instances from suppurative inflammations of lymph-glands which have received their infection from carious teeth or affections of the tonsils, ears, mastoid, scalp, face, etc. Sometimes wounds of the skin or adjacent mucous surfaces, or even pyemia, may be the source of bacterial invasion.

Firm layers of deep fascia divide the neck into various "spaces" which determine to a large extent the location and mode of spreading of suppurative inflammations. The two most important of these spaces, owing to the lymph nodes which they contain, are the one surrounding the large vessels and the one occupying the submaxillary region.

Perhaps one-half of all deep cervical abscesses are found in the submaxillary region. Next in frequency are those about the great vessels. If a submaxillary abscess is external to the capsule of the salivary gland the symptoms are not profound and the danger not great; but if it is intracapsular the symptoms become extremely serious from the tension under which suppuration takes place, even gangrene resulting at times. Although the skin is not involved early, there is great swelling and difficulty in respiration and deglutition, with rigors, high fever, and profound sepsis. This is known as *Ludwig's angina.*

Deep-seated abscesses of the neck are always serious on account of the complications which may arise, such as diffuse cellulitis; extension into the mediastinum; or rupture into the great vessels, the trachea, esophagus, or pharynx. In the phlegmonous form, death may even result before suppuration appears, so intense is the septic poisoning.

Incision should be promptly resorted to and thorough drainage instituted. Skin incisions should be made as far as possible in the natural wrinkles of the neck, so as to avoid unsightly scars, and the blunt method of penetrating the deeper tissues should be employed (Hilton's method). If much gravitation of pus has occurred, counter-openings should be made. Serious secondary hemorrhage must be met by ligation, if possible, rather than relying upon a tampon.

Ligneous Phlegmon, or Abscess, of the Neck.—This is an extremely chronic suppurative inflammation of the subcutaneous cellular tissues of the anterior and lateral aspects of the neck, although it occurs rarely elsewhere, for instance, in the abdominal wall following appendicitis. It was first described by Reclus in 1894. A board-like hardness of the tissues gradually develops, confined, perhaps, to a limited area, but often enveloping the larynx and trachea and even extending into the floor of the mouth. This consists of inflammatory exudate and fibrous tissue, and in it finally appear numerous small, ill-defined abscesses, or possibly large collections of pus due to coalescence of smaller ones.

The disease develops so remarkably slowly that weeks and even months may elapse before suppuration manifests itself. For a long time there are none of the usual signs of inflammation—no tenderness, heat, pain, or redness,—simply an indurated board-like swelling. Later, the skin becomes involved, pits on pressure, and assumes a reddish-violet hue, like the cutaneous surface of a carcinoma. The movements of the head may become restricted, but not from pain as much as from induration and infiltration of muscles and subcutaneous tissues.

The *causation* is obscure. Although the ordinary pus-forming microorganisms are usually present, other germs have been demonstrated, such as the diphtheria, pseudo-diphtheria, and typhoid bacilli, the pneumococcus, the ray fungus, the colon bacillus, etc. The assumption of Reclus is probably correct, that this peculiar disease has no specific cause, but is due to the presence of germs of weakened virulence acting upon tissues with high resisting powers, which throw up unusual barriers against microbic invasion. Against the theory of resistance of the tissues, however, is the fact that the disease is usually found in weakened and cachectic individuals. It is likely that the process begins in the lymph-glands, which are in communication with the mouth and nose, and it is possible that it may be kept up by repeated infections from this source. Syphilis should always be suspected. Lang's opinion that ligneous phlegmons are always due to epitheliomatous infiltration is not shared by others and has not been substantiated clinically.

The *diagnosis* is difficult, as may be appreciated from the fact that ligneous phlegmons are nearly always mistaken for carcinomatous or possibly tuberculous infiltrations arising from the cervical glands. Even the advent of suppurative foci does not always settle the question, as these appear sometimes in connection with cancer; so that in order to be certain in such a case one would have to wait until the patient recovered, which might require three or four months. The reddish-violet color of the skin and the extensive board-like induration resemble very closely cancer *en cuirasse*, and the similarity is strengthened by incision into the carcinomatous-like tissues.

The *treatment* is not very satisfactory. Reclus warns decidedly against attempted extirpation of the diseased area, as this is well-nigh impossible. Hot fomentations can be employed and abscesses opened as they present themselves; but the incision of a few small purulent foci seems to have but little effect upon the progress of the disease. Nevertheless multiple incisions can be tried. Everything possible should be done, however, to build up the resisting powers of the body, by means of tonics, food, hygiene, etc. The presence of diphtheria bacilli would, of course, indicate the use of antitoxin, and iodid of potassium should be employed whenever syphilis is suspected.

Retropharyngeal or Postpharyngeal Abscess.—This may be either acute or chronic. The *acute form* arises from injury to the pharynx by swallowing some sharp object or a corrosive chemical; or, in children, from inflammation of prevertebral lymphatic glands following a severe angina, such as often occurs in the acute exanthemata. Pyemia, mastoiditis, and acute osteomyelitis are also occasional causes.

The *chronic form* is practically always tuberculous, and is due to caries of the upper cervical vertebræ or base of the skull, and sometimes to caseous degeneration of lymph nodes. The pus may burrow along the front of the spine into the posterior mediastinum and even appear eventually as a psoas abscess.

A retropharyngeal abscess forms a fluctuating swelling of the posterior pharynx. In the acute form and in mixed tuberculous infections dangerous edema of the adjacent parts, including the glottis, may arise and be accompanied by severe constitutional symptoms.

The only *treatment* is prompt evacuation of the pus, especially in acute cases, preceded, perhaps, by hot or cold fomentations or an ice-bag applied to the neck when indicated. The incision was formerly made through the mouth by means of a well-guarded bistoury; and even at the present time there are circumstances in which this may be desirable, particularly if it is done under cocain or in the Trendelenburg position, so as to prevent strangulation by the escaping pus. The better method, however, in almost all instances, is to enter the abscess by means of blunt dissection from the external surface of the neck along the posterior border of the sterno-mastoid muscle, thus avoiding the dangers of aspiration pneumonia, mixed infection, and defective drainage.

Palmar Abscess.—These serious abscesses generally originate in an inflammation of the fingers, usually the little finger or thumb, which have tendon-sheaths continuous with that of the palm, whereas the tendon-sheaths of the other fingers have no such connection. The infection, however, may enter more directly, from injuries, blisters, cracks in the skin, or from inflammations in connection with callosities of the palm.

When the suppuration is beneath the palmar fascia the local and general disturbances are usually great. The entire hand swells enormously, including the back of the hand and the fingers, the latter becoming flexed and immovable. The pain is intense and throbbing. If the pus is not speedily evacuated, it may burrow through between the bones to the dorsum of the hand, or along the tendon-sheaths into the forearm.

Owing to the depth of the inflammation redness of the skin does not appear early and should not be considered in the diagnosis, which must be based on the history, pain, swelling, and constitutional symptoms.

When the disease is severe or neglected, contractures of the fingers, stiffness of the joints, and a glazed, sensitive condition of the skin with poor circulation may result, rendering the hand more or less useless. In order to prevent this unfortunate sequel, as well as the danger of sepsis, early incision under anesthesia is imperatively demanded, with due regard to the various "spaces" or "pockets" which limit the purulent collections. The palmar arch lies at about the level of the web of the thumb, hence the longitudinal incision should be made as far as possible distalward from this. When required, the wrist and arm must also be opened. Knavel advises an incision along the lateral aspect of the wrist through which the pus may be reached by burrowing beneath the tendons next the bone. Amputation is seldom indicated. The production of passive hyperemia by elastic constriction of the arm, as suggested by Bier, may be of service. (See Treatment of Acute Abscess.)

The best after-treatment consists in the free use of hot mild antiseptic baths and fomentations, followed later by passive motion and massage.

Felon, Whitlow, Paronychia, or Panaritium are terms applied to infections of the fingers or thumb, particularly the palmar surfaces of the terminal phalanges. Theoretically there are several distinct forms, although clinically these are difficult to differentiate. The process may attack the skin alone, forming a purulent blister only; or it may involve the subcutaneous cellular tissues, like a boil; or the tendon-sheaths may become infected, or even the periosteum, resulting in necrosis of the bone.

The perpendicular arrangement of the subcutaneous fibers seems to direct infection to the deeper parts; while the tendon-sheaths, lymphatics, and even the veins may carry it rapidly into the palm of the hand, the forearm, or the lymph nodes of the elbow or the axilla. In this way extensive, wide-spread, and dangerous suppurations result from apparently trivial injuries, such as the prick of an infected needle, which may have healed before the more serious damage appears. Infections of the little finger and thumb are more dangerous than those of the remaining fingers, because their tendon-sheaths are continuous with those of the palm and forearm, the other tendon-sheaths forming closed sacs terminating more or less definitely at the metacarpophalangeal articulations.

A so-called *shirt-stud* or *collar-button abscess* is a panaritium in which a superficial collection of pus is connected with a deep one by means of a small opening through the deep fascia. The name is also applied to similar abscesses in other regions and in bones.

Although many felons appear to originate spontaneously, and perhaps some do, the great majority arise from slight and possibly unnoticed injuries. The finger soon becomes dusky-red, swollen, and very tense, and is the seat of excruciating throbbing pain, particularly if it is allowed to hang down or is struck against something. When the process is subperiosteal, the pain and constitutional symptoms are greatest. Pyemia or septicemia may result.

Valuable time should not be wasted with attempts at abortive *treatment*, although in the very beginning hot fomentations may be of some service. *Early incision is strongly indicated* in order to prevent spreading of the infection, necrosis of the bone, or even death of the individual. In the deep-seated forms the cut should penetrate to the bone; but in the superficial varieties it should not be so extensive, as it would be unwise to open the non-infected tendon-sheaths. When the sheaths are involved, however, it may be necessary to slit them up as far as the pus extends, or at least make ample counter-openings further down the finger. Necrosis of tendons may result. A primary amputation of the finger should seldom be done. In some forms of infections of the fingers, which exhibit little or no tendency to the formation of pus, such as certain postmortem and dissecting wounds, it may be unwise to incise too quickly for fear of opening up fresh channels of infection and thus aggravating the condition.

The *after-treatment* consists in the application of hot moist fomentations or the warm antiseptic bath (boric acid solution or bichlorid, 1 : 20,000). Passive congestion produced by elastic constriction of the arm may be of service. (See Treatment of Acute Abscess.)

Abscess of the Breast may occur superficially, in the subcutaneous cellular tissues (*supramammary*); within or between the lobules (*intramammary*); or in the cellular tissue beneath the breast (*submammary or retromammary*). In the two varieties first mentioned the microörganisms enter through the lymphatics leading from an ulcerated or fissured nipple, or possibly through a lacteal duct. In the remaining form the infection comes secondarily from the breast itself, from a diseased rib, from pyemia, or from an injury.

Suppurative mastitis is seen most frequently in women during lactation, although it occasionally occurs at other times, especially shortly after birth and at puberty. It is rarely seen in males. The superficial variety is nothing more than an ordinary boil, but the deeper forms are often serious affections accompanied by marked constitutional symptoms.

Pus within the breast-tissues forms a single large abscess or a number of smaller ones which may coalesce later on. If left to itself, the abscess may burrow to the surface, leaving fistulæ which are difficult to heal. The entire breast can thus be ruined functionally and cosmetically. Enlargement of the axillary and the supraclavicular glands is not uncommon. The mamma soon becomes swollen, tense, and tender, and the seat of severe throbbing pain; redness and infiltration of the skin occurring later. One or more nodules of induration can be detected on palpation, but fluctuation is difficult of demonstration.

When the purulent fluid lies beneath the breast, the whole gland is pressed forward, the nodular feel being absent.

The *treatment* of the intramammary form consists in the application of hot fomentations in the early stages, followed by prompt evacuation of pus under an anesthetic as soon as there is reason to suspect its presence. The incisions should radiate from the nipple and should be free. Separate pockets must be broken into with the finger.

In very severe cases, with multiple abscesses and profound septic infection, immediate amputation of the breast may be called for.

The submammary variety is most advantageously opened by an incision in the crease between the lower border of the gland and the chest wall. Suitable cases of intramammary abscess may be approached through a similar incision, by elevating the breast and burrowing into its substance from beneath.

Axillary Abscesses.—These may be either superficial or deep. The *superficial suppurations* are in the nature of furuncles, and arise frequently from infection through a hair-follicle or sebaceous gland. They have a tendency to appear several at a time, and to recur at greater or lesser intervals. Extensive and annoying infiltration of the skin may result.

Deep suppurations are nearly always glandular in their origin, the germs entering through the lymphatics from the upper extremity, especially those from the fingers. The breast, the pectoral region, and the axilla itself are also sources of infection. Sometimes an abscess arises from diseased bone or from the shoulder-joint, and rarely gravitates from the neck.

Periadenitis readily occurs, from bursting of the glandular capsule, and an extensive phlegmon may follow, which at times burrows under and between the pectoral muscles very extensively. In such instances septic poisoning is marked, as it sometimes is even when the process is confined to the lymph nodes themselves.

In *opening an axillary abscess*, which should be done as soon as there is reasonable presumption of the existence of pus, the arm should be elevated and a cutaneous incision made midway between the axillary folds, on the side of the chest if possible, and from above downward. The pus cavity should then be bored into with hemostatic forceps, according to the method of Hilton, in order to avoid injuring the axillary vessels and nerves. Care should be taken not to open into an aneurism surrounded by pus, as has sometimes been done.

Abscess of the Lung is due to a variety of causes—pneumonia, particularly that arising during the course of influenza; embolism; foreign bodies; wounds; perforation of neighboring foci of suppuration, such as subphrenic or hepatic abscesses; tuberculosis, etc.

The *diagnosis*, including the location of the abscess, is often extremely difficult. It is made from the history and the physical signs, and especially from the periodic expectoration of quantities of pus perhaps containing shreds of lung tissue or elastic fibers.

Treatment is most apt to be successful in cases following pneumonia. In general, it should be operative, although cases occasionally recover spontaneously, especially those situated in the upper portion of the lungs, which drain more effectively into the bronchi. Early operation is desirable because the walls of the cavity so thicken with time that satisfactory recovery is difficult. Exploratory punctures are not advisable unless the pleuræ be adherent, which should always be determined before operation, if possible, in order to guard against fatal collapse of the lung when the thoracic wall is opened. Collapse may be prevented in any case by use of the Fell or the Matas apparatus for maintaining expansion of the lung, or the Sauerbrunn pneumatic chamber; and sometimes the same end may be attained by suturing the lung to the parietal pleura or by rapidly grasping it with forceps after opening the chest wall.

Irrigation of the abscess-cavity should not be practised, for fear of inundating the bronchi, and drainage-tubes should be moved frequently to avoid erosion of blood-vessels. When an abscess is situated in a lower lobe, it has been suggested that the foot of the patient's bed be elevated sufficiently to encourage bronchial drainage.

Mediastinal Abscess is an extremely serious although rare affection, often causing death by sepsis or pressure. It generally arises from suppuration in neighboring regions, especially the neck and the bodies of the vertebræ. It may also be caused by lesions of the lymph-nodes, esophagus, lungs, pleura, pericardium, ribs or sternum; while trauma, pyemia, and certain acute diseases are less common causes.

Pain, beneath the sternum and in the back, is the most prominent symptom. Pressure-signs are often striking and suggestive, such as dyspnea, irregular heart, etc.

The abscess may present in an intercostal space or break into the trachea, the esophagus, the pleura, or the pericardium.

Early evacuation of pus is necessary in nearly all cases to obtain a cure. If the abscess point between the ribs, this is easy; if it does not, then, when the difficulty is in the anterior mediastinum, the sternum must be trephined or a portion removed; and when it is in the posterior, a trapdoor must be turned back from the ribs near the spine in order to reach the seat of the abscess—a serious and difficult operation at best.

Subphrenic (Subdiaphragmatic) Abscess ("*Pyopneumothorax subphrenicus*"—Leyden).—Formerly more or less of a clinical curiosity, from its supposed rarity and the difficulty of diagnosis, it has recently grown much in importance with the advance of abdominal surgery, especially that of the appendix and stomach. It was described by Barlow in 1845, the first operation being recorded by von Volkmann, in 1879. The comprehensive articles of Leyden and Maydl served to direct attention to the subject.

Definition.—An abscess beneath the diaphragm and in contact with it at some point. It is in the majority of instances really a localized peritonitis of the upper portion of the abdominal cavity, although it is often subperitoneal, and rarely it occupies the substance of the diaphragm itself. It frequently involves adjacent organs, particularly the liver.

Causes.—These are numerous and varied. In fact, anything capable of producing local peritonitis beneath the diaphragm may give rise to subphrenic abscess. The most frequent causes, however, are perforations of the stomach and duodenum (70 out of 214 cases—Perutz), and appendicitis (55 out of 214). Following these come affections of the liver, such as abscess, suppurative cholecystitis, etc. To these may be added perinephritis, purulent diseases of the spleen, pancreatitis, perforation of the transverse colon, empyema thoracis, purulent pericarditis, peri-esophageal suppuration, tuberculous and other affections of the ribs and vertebræ, together with trauma, furunculosis, and various indefinite and obscure causes which cannot be tabulated. Not infrequently a subphrenic abscess represents the remnants of a general peritonitis.

Situation and Boundaries.—These vary according to the cause. With the suspensory ligament of the liver as a dividing-line, those abscesses of hepatic, appendical or duodenal origin are found to the right of the ligament; while those arising from perforation of the stomach or inflammation of the spleen or pancreas are found to the left. The transverse colon with its mesentery forms a partition which limits the extension of the inflammatory process downward, the colon and adjacent omentum becoming adherent to the anterior parietal peritoneum. So firm are these adhesions that perforations into the peritoneal cavity seldom occur.

In a general way, it may be said that perforating ulcers of the anterior wall and greater curvature of the stomach are apt to give rise to general peritonitis, while those of the lesser curvature and posterior surface lead to the formation of subphrenic abscesses. Their boundaries vary so much that it is useless to attempt to classify them with accuracy, but nevertheless three more or less well-defined "spaces" are recognized (Legars): (1) between the diaphragm above and the liver below (due to perforation of the stomach alone); (2) between the diaphragm and outer part of the left lobe of the liver superiorly, the stomach and pancreas internally, the ribs, spleen, and diaphragm externally, and the colon and its mesentery inferiorly (usually of splenic origin); (3) posterior to the stomach, in the bursa omentalis or subperitoneal sac (from the stomach or the pancreas).

Abscesses arising from the gall-bladder or duodenum, accordingly as they are more superficially or deeply situated in the beginning, may pass anteriorly or posteriorly to the liver, thus reaching the diaphragmatic vault.

An interesting division, of greater theoretic than practical value, is into extraperitoneal and intraperitoneal abscesses. As a rule, the former arise from parts without the peritoneum, such as the kidneys and ribs, and the latter from organs within it, although there are many exceptions. An extraperitoneal collection of pus frequently becomes intraperitoneal by perforation, because the connection between the diaphragm and peritoneum is such as to preclude the formation of a large abscess. Abscesses arising from the appendix, like those from the stomach and duodenum, are sometimes extraperitoneal and sometimes intraperitoneal according to circumstances. A general peritonitis of appendical origin may leave behind it a subphrenic focus; or the infection may pass upward within the peritoneum, perhaps external to the colon, but limited by adhesions, until the diaphragmatic surface of the liver is reached. On the other hand, the subperitoneal lymphatics are frequently the conducting agents, as has been demonstrated experimentally by means of colored fluids (Sanger, Körte) as well as clinically. When this occurs, an appendical abscess usually exists either intraperitoneal or subperitoneal or between the leaves of the mesentery of the appendix; although the presence of such an abscess is not necessary. Among 600 cases of appendicitis occurring in Sonnenberg's clinic, in Berlin, were found 9 subphrenic abscesses.

Complications.—The most frequent and important of these is pleurisy with effusion, either serous or purulent. It occurs in from one-half to two-thirds of the cases. The infection may take place in several ways: (1) through the blood; (2) through the lymphatics, although direct lymphatic connection has been denied; (3) directly, by contiguity; and (4) by way of the cellular tissues outside the peritoneum and pleura, through openings in the diaphragm, and involving the pleura secondarily, by perforation or otherwise. The two ways last mentioned are by far the more common, the one selected varying according to the intraperitoneal or extraperitoneal situation of the primary purulent focus.

Pericardial inflammations and mediastinal suppurations may also occur, as well as abscesses of the lung and liver, while perforations into the bronchi take place fairly frequently.

Contents.—The *pus* varies in its characteristics as does pus elsewhere, although it is often influenced by the origin of the abscess; for instance, it may contain bile, liver cells, ecchinococcus cysts, carious bone, caseous débris, or rarely stomach contents. When the appendix is at fault the pus is usually characteristically foul in odor.

A striking feature of subphrenic abscess is the presence of *gas* or *air* in approximately one-half of the cases. In fact, the cavity may be almost filled with gas and contain so little pus that it cannot be detected with an exploring needle. It was formerly thought that this gas invariably came from perforation of the stomach or intestines, or possibly the lungs. Although this is undoubtedly true at times, a more rational explanation is that it is in the majority of instances of microbic origin, as in ordinary appendical abscesses. When gas and pus are both present, the former always seeks the higher portion of the cavity and the latter the lower, their relations varying with the position of the patient.

Many forms of *microörganisms* have been found, the most characteristic feature in this connection being the frequent presence of the colon bacillus when the lesion is of appendical origin.

Symptoms and Diagnosis.—As in local peritonitis elsewhere, the symptoms vary from mild to stormy. They are occasionally so insignificant as to escape detection, there being practically no rise in pulse or temperature and no leukocytosis. Again, when due to sudden perforation of the hollow viscera, they are so severe as to produce collapse.

Among the early symptoms may be mentioned shallow respiration and cough (due to irritation of the diaphragm), pain, tenderness, perihepatitis (with characteristic friction sounds), fever, chills, and sweats.

The frequency with which perihepatitis, the first stage of subphrenic abscess, occurs in connection with appendicitis is worthy of note. It often, however, undergoes speedy resolution.

In more advanced cases, where the abscess cavity is of considerable size, the symptoms are more marked, although often difficult or impossible to interpret correctly. There is occasionally bulging of the intercostal spaces, or even of the chest wall itself; and when the purulent collection is appropriately situated, it may cause swelling below the border of the ribs or in the loin or epigastrium, or it may depress the stomach or bulge it prominently forward. Local edema may be present, especially in the loin.

The liver is often more or less depressed, sometimes well below the umbilicus, and its width apparently increased by the collection of pus above.

The greatest difficulty in diagnosis is in the *differentiation of a subphrenic purulent collection from a pleuritic effusion*, especially if the latter is supposed to be encapsulated at the base of the pleural cavity. The pressure of an abscess is apt to cause a local upward curve or "cupping" of the diaphragm which may rarely reach the third and even the second rib and can be detected by auscultation and percussion. It should be noted that breath-sounds can often be heard in modified form well into the dull or tympanitic area of an abscess, and if the diaphragm is movable their audibility downward may be increased on deep inspiration. The line of dullness beneath a large quantity of fluid in the pleura, on the other hand, is apt to curve downward, if it vary from the normal at all, and the breath-sounds cease abruptly. The presence of respiratory mobility of the lung should be noted in abscess, but the "diaphragm phenomenon" of Litten is not of much diagnostic importance. There is no change of level of the fluid with variations of the posture of the patient unless gas be present, and then these variations are significant and marked, and confined to a space beneath the diaphragm. The lateral displacement of the heart so often seen in extensive pleuritic effusions does not occur, although it may be more or less pushed upward and perhaps slightly outward.

The insertion of an *aspirating needle* into the pus-cavity can give important information regarding the seat of the trouble. If the fluid is subphrenic and the diaphragm is penetrated, the needle may move up and down with respiration, while the fluid will flow more freely on inspiration than expiration. If the cavity should contain air or gas, the effects of respiration may be noted upon the flame of a candle held close to the opening of the needle, remembering that the gas will sometimes become ignited (Weir); or the end of the needle may be immersed in sterile water, thus rendering visible the expulsion of gas when the diaphragm descends.

Unfortunately, however, the value of all signs depending upon movements of the diaphragm is frequently interfered with by paralysis of that muscle due to inflammation or upward pressure of the effusion. Extensive adhesions to the parietal pleura within the cavity of the chest will produce the same effect. The latter complication may also prevent the obtaining of different fluids at different depths, as may occasionally be done when pleurisy and subphrenic abscess coexist; or it might obscure that sense of distinct resistance when the needle passes from the cavity of the pleura through the diaphragm into the subphrenic cavity, which has frequently been dwelt upon as an important sign.

When both serum and pus, that could not come from the same cavity, are obtained at different vertical levels during aspiration, it is suggestive of subphrenic abscess in conjunction with pleural effusion, although not positive, because of the possible existence of separate encapsulated pleural foci.

When the abscess-cavity contains a considerable quantity of gas it may closely simulate a pneumothorax; but the limitation of the tympany to the lower portion of the chest, the lack of abrupt cessation of breath-sounds, and the bulging upward of the diaphragm at one point, together with the inability to cause a variation in the upper border of the tympanitic zone by changing the position of the patient, should lead to a suspicion of the true condition. Such changes of position may cause, however, comparative variations of dullness and tympany *below* the diaphragm, owing to shifting of the fluid contents of the abscess. It should be noted that percussion and auscultation under these circumstances reveal from above downward three sharply defined zones—the normal lung, a collection of gas, and a collection of pus, the location of the pus varying with the patient's position, although never causing dullness above the diaphragm. If there is, in addition, an effusion in the pleural cavity, four zones are present (lung, fluid, gas, fluid), the level of the second one being variable, that of the third constant, and that of the fourth variable. In estimating the value of these various signs, the possibility of confusion arising from a stomach containing fluid and dilated with air must sometimes be excluded by the use of the stomach-tube.

The history of the case is of service, especially as to whether the disease was preceded by symptoms within the abdomen or within the chest, and the X-ray may occasionally be of assistance in establishing a diagnosis.

Prognosis.—Although this is serious enough under any circumstances, it is much improved by early diagnosis and operation. According to the nature and mode of infection, the patient may die in a few days or even hours, or he may linger for weeks or months. Resolution sometimes occurs, especially in abscesses of tuberculous character, but it is very uncommon. Rupture rarely takes place externally or into the stomach, bowels, or peritoneum. It may occur into the bronchi directly, or indirectly by way of the pleura, and recoveries sometimes result in this way. Rarely abscesses have emptied themselves into the pericardium with fatal results. Death is usually due to sepsis.

The *mortality* varies considerably according to the origin of the abscess, being higher in perforations of the stomach than in appendicitis. It also varies with the time of operation. According to the statistics of Sachs, when operated on within three weeks, 15.3 per cent. of cases died; but if operated on later the mortality was 50 per cent.

The general mortality is placed by Maydl at 56 per cent.; and by Elsberg at 40 per cent. With operation, the mortality, according to Grüneisen, is 33.5 per cent.; Maydl, 35.7 per cent.; Sonnenberg, 42 per cent.; Sachs, 37.5 per cent.; and Elsberg, 22 per cent. Sonnenberg places the mortality of unoperated cases at 55.5 per cent.; Sachs, 71.5 per cent.; and Elsberg, 82 per cent.

Treatment.—There is no question that subphrenic abscesses are often prevented by timely operation on various abdominal lesions, such as appendicitis, ulcer of the stomach, abscess of the liver, etc. In appendicitis, however, this is not always true; because subphrenic infection may take place apparently in the very beginning of the appendicular inflammation, before the formation of pus.

In order to get the best results, collections of pus beneath the diaphragm should be opened early and drained freely. Simple aspiration is useless. Owing to difficulties in diagnosis, many cases reach the surgeon so late and in such poor condition that it may be wiser, in rare instances, to employ local rather than general anesthesia. It is seldom expedient to search for perforations of the stomach or to attempt the removal of a diseased appendix. The surgeon should aim at thorough drainage only, and reserve secondary operations for some future and more favorable time. This does not apply, however, to the opening of abscesses wherever they may be found or to the drainage of the pleural cavity when necessary.

Before operating it is almost always advisable to explore with an aspirating needle; but owing to the danger of phlegmonous inflammation along the puncture, the complete operation should follow immediately when pus is found.

Even when the abscess is penetrated, little if any pus may be obtained, owing to its thickness or to the preponderance of gas in the cavity. Hence it is well to inspect the caliber of the needle carefully for traces of pus which would otherwise escape detection. Beck even advises washing out the needle with sterile water and applying the culture test.

Operation may be done entirely below the diaphragm and pleura; for instance, in the loin, below the costal margin, or in the epigastric region, according to the position in which the abscess presents itself. A few operators prefer to employ the infracostal route in all cases. Or the eleventh and twelfth ribs may be resected and the pleura pushed up, according to Lannelongue. Or the operation may be done, as is usually preferable, owing to the high situation of the pus-cavity, by resecting one or more ribs and perforating the diaphragm as it arches upward beneath the lower portion of the thorax. This is very simple when the surfaces of the pleura are adherent, as they often are; but when this is not the case, the procedure is more difficult and complicated.

Theoretically, the best technic is that used by Elsberg. About two inches of the ninth and tenth ribs are resected somewhere between the scapular and the anterior axillary lines. The reflection of the pleura usually lies in the center of the wound, provided the thoracic cavity has not been carried downward by extensive effusion or upward by adhesions. Hence, when desirable, the pleura may be avoided altogether, the abscess being opened below it, while again it may be conveniently drained through the upper portion of the wound and the abscess through the lower. Practically, however, the incision must often be made directly through the free pleural cavity; but the danger is much lessened in the majority of instances by the close application of the visceral membrane against the parietal, especially if an assistant presses the liver firmly upward. With a free opening it is not difficult to sew the surfaces of the pleura together with a running "back-stitch," reinforcing the suture line with gauze. Operating in two stages is unnecessary, as a rule, although it may at times be advisable. Drainage should be by tubing rather than gauze. A counter-opening in the loin is desirable when it can conveniently be made. A coexisting *empyema* always requires drainage, unless it be purely tuberculous, when a question may arise. Such drainage can usually be obtained through the original wound, although expediency may call for an opening in some other situation.

Abscesses of the Liver.—These may be single or multiple, large or small; the large solitary form being usually known as "tropical abscess," although often found elsewhere than in the tropics. Multiple abscesses are frequently pyemic.

The most prominent *cause* is some inflammatory trouble in a region drained by the portal system of veins—generally an amœbic dysentery; possibly an appendical abscess, suppurating hemorrhoids, septic phlebitis, or other intestinal, peritoneal, or vascular inflammation. Further causes are cholecystitis, cholangitis, perforating ulcer of the gastro-intestinal tract, empyema, pyemia, infected hyatid cysts, etc.

When the *symptoms* are pronounced, the diagnosis is comparatively easy, —irregular fever with marked rise and fall, chills and sweats, emaciation, pain and heaviness in the right hypochondrium and shoulder, enlargement of the liver, bulging of the ribs, perihepatitis, irritation of the diaphragm, leukocytosis, etc. But cases are not infrequent where the symptoms are so obscure that a diagnosis is almost impossible. Fever, pain, chills, and sweats and all local signs may fail, and there may even be no marked increase in the number of leukocytes. The patient merely loses flesh and does not feel well in various ways. Between these extremes lie many intermediate forms.

In attempting a *diagnosis* it is often justifiable to use an aspirating needle—not only once, but many times in succession—providing an operation is done as soon as pus is found.

The only *treatment* of tropical abscesses is by operation, but with multiple abscesses little or nothing can be accomplished. Aspiration is sometimes advised, but it is usually ineffective. In operating, there is no difficulty if adhesions to the parietal abdominal wall have formed. If these are lacking, however, it will be necessary to pack with gauze; when the abscess may either be opened at once or left until firm adhesions develop. The opening may be made with the knife, with some blunt instrument, or with the thermocautery. Hemorrhage is controlled by packing.

Appendical Abscess.—This is usually due to perforation or gangrene of the appendix, although it may originate from migration of bacteria through the unbroken covering of the organ. The walls of such an abscess are usually formed of omentum and intestine glued together by peritoneal exudate, together with more or less of the parietal peritoneum. Sometimes the abscess is within the mesentery of the appendix or in the cellular tissue beneath the peritoneum. The pus is usually foul, and the cavity often contains gas from the growth of the colon bacillus. If left to themselves such collections of pus may break into the peritoneal cavity, bowel, bladder, or other hollow viscera, or burrow internally in various directions. They often give rise to serious septic complications.

In addition to the constitutional *symptoms* of suppuration, local muscular rigidity is a prominent feature, and tumefaction is usually but not always to be felt. Fluctuation and local edema are present in the later stages only, and should not be depended upon in diagnosis. The nearer the abscess is to the anterior parietal peritoneum, other things being equal, the more prominent the local signs. Those situated beneath the lower border of the liver or below the brim of the pelvis are often extremely difficult to detect.

An appendical abscess should be opened under local anesthesia if a general anesthetic is contraindicated. An important question is *when to operate.* Many surgeons advise operating at any time, as soon as the case is seen, while others prefer, with certain exceptions, to delay operation until the adhesions have become sufficiently strong to resist careful manipulation, say on the sixth or seventh day, the patient being starved in the meantime, for the purpose of controlling peristalsis (Ochsner). In order to protect the peritoneal cavity, gauze packing must be freely used when necessary. Drainage is better obtained with rubber tubing than with gauze.

Perirenal or Perinephric Abscesses.—These may be *primary* and due to trauma, including blows, strains, and other injuries; or to sudden chilling or great heat, especially if accompanied by exhaustion; or to the exanthemata; or to metastasis. Or they may be *secondary* to suppurative disturbances of the kidney or adjacent parts, such as the appendix, gall-bladder, vertebræ, etc. Sometimes there is no apparent origin, when they are known as "idiopathic."

When an abscess of the kidney is the cause, the infection may travel through the capsule by way of the lymphatics or directly by perforation.

One large abscess, perhaps in "pockets," may exist, or numerous small ones. Sometimes several pints of pus are found. Extraordinary amounts of hard fibrous tissue may form around an abscess of small size so as to simulate a solid tumor of the kidney and greatly embarrass attempts at enucleation of the organ.

The *symptoms* are often obscure, so much so, in fact, that perinephric abscess may be overlooked in the presence of the trouble which has given rise to it. There may be nothing but an obscure fever, resembling typhoid perhaps, with so few local indications that they do not attract attention. Usually, however, there are local tenderness and pain, together with muscular rigidity and perhaps swelling and edema in the loin. Fluctuation seldom occurs, owing to the depth of the suppuration and the resistance of the parts. The pain may radiate down the limb or into the bladder or testicle, and is often severe. The thigh is frequently flexed on the pelvis and the body bent to the affected side, leading to a peculiar and awkward gait. The foot and leg may be swollen. The character of the urine aids but little in the diagnosis unless the kidney be involved.

Treatment consists in evacuation of the pus through a lumbar incision such as is employed for nephrotomy, followed by ample drainage. If pockets exist, they must be broken into from the main cavity. A fistula may remain, even though the kidney is not involved, owing to rigidity of the overlying ribs and the movements of respiration.

Ischiorectal Abscess, a form of periproctitis, occurs in the cellular tissues of the ischiorectal fossa. It generally arises from infection from within the bowel, from lesions of the perineum, the prostate, or the urethra, from collections of pus which have burrowed down from above, or possibly from trauma or metastasis. The foul odor of the pus is due to the colon bacillus, which escapes from the bowel through an abrasion, an ulcer, an inflamed gland or pile, or through the lymphatics alone. They are often tuberculous. Chiari has called attention to the frequent existence of abnormally deep *lacunæ Morgagnii*, which form little diverticula or pockets just above the anal sphincter. He considers that infection of these diverticula is the most common cause of ischiorectal abscess.

When the process is superficial it is easily detected by the local and general symptoms of an abscess, but when it is more deeply seated its presence is not so manifest. A painful resistance, however, can be detected when compared with the opposite side, within the bowel if not externally. Defecation often causes much suffering, and it is difficult for the patient to sit with comfort. As the abscess develops, the induration increases until it sometimes involves a large area, the skin becoming brawny and reddened. Fluctuation may appear, and finally the pus breaks into the bowel or externally. Whether the abscess evacuates itself without or within, or in both directions, a fistula often results, which will seldom heal until the sphincter muscle is divided by operation. Occasionally diffuse cellulitis or gangrene of the skin results, especially in the old or debilitated or in abscesses following an injection-treatment for piles.

The constitutional *symptoms* vary from disturbances which are trivial to severe septic poisoning with typhoidal manifestations.

If the abscess is opened early, before it perforates the bowel or approaches it too closely, a fistula may often be avoided. The incision should be free and from the skin-surface, never from within the bowel, and the drainage adequate, a soft-rubber tube rather than gauze being employed.

Abscess of the Prostate is, in the great majority of instances, of gonorrheal origin, although it may originate from other inflammations of the bladder or urethra, or from catheterization, metastasis, etc. Tuberculosis is a common cause. Trauma, such as arises from horseback-riding, is probably responsible for few cases unless some other cause already exist.

These abscesses may be single or multiple and they may occupy one or more lobes. They may break into the urethra, the bowel, the bladder, or externally through the perineum. They rarely cause peritonitis. Stubborn fistulæ sometimes remain, which may even connect the bowel with the urinary tract. Periprostatic cellulitis of a severe type occasionally develops.

Pain is a prominent symptom. It is felt in the prostatic region or in the rectum, especially during defecation or the passage of urine. The perineum is tender and possibly swollen, and the enlarged and sensitive prostate can be felt by a finger in the bowel. The passage of a catheter, which may be necessary in retention of urine, is exquisitely painful.

The general symptoms are frequently but not always marked. There are apt to be high temperature, chills, and occasionally profound septic manifestations, among which a dry tongue and delirium are prominent.

It is occasionally possible to open a prostatic abscess by manipulating a metallic catheter within the urethra; but usually an incision is required, preferably through the perineum, possibly through the bowel. This should be done early, to control sepsis and prevent the formation of fistulæ.

Abscess of the Groin or Bubo.—These collections of pus almost always arise from inflammations of the lymph-glands, except in the case of psoas abscess of tuberculous or other nature, and abscesses originating within the pelvis and pointing in the inguinal region.

The *glands of the groin* are both superficial and deep. The former, eight or ten in number, form two more or less distinct sets; one set being arranged parallel to and below Poupart's ligament, with their long axes transversely, and the other set collected about the saphenous opening, with their long axes vertical. The first set receives the lymphatics from the genital organs, perineum, gluteal region, and lower abdominal wall; while the second is in communication with the lymphatics of the entire lower extremity. The deep nodes lie around the great vessels, beneath the deep fascia, and communicate with the superficial nodes through the saphenous opening. The gland lying within the femoral opening (Rosenmüller's gland) has received special attention.

Causes.—As soon as a bubo is detected, the source of infection should be sought for; remembering that it may be small, a mere abrasion, and possibly healed and forgotten before glandular suppuration takes place. The familiar red streaks indicating involvement of lymphatic vessels are often absent. Upon the lower extremity the original focus is most frequently found about the toes, produced, for instance, by the careless paring of a corn.

The most common location of the original lesion is, however, the genitalia, especially the vicinity of the frænum. Such infections are usually specific,—chancroid, gonorrhea, syphilis,—but they are not always so, being sometimes due to balanitis or to a simple abrasion. It has been estimated by Petzold that buboes complicate 75 per cent. of soft chancres, that 25 per cent. of these suppurate, and that 10 per cent. to 15 per cent. of those which suppurate are "virulent," that is, contain active, inoculable chancroidal poison. Such an estimate as this, however, is merely relative, for it does not follow because a bubo arises from a specific lesion that it is itself specific. In fact, the pus from such a bubo may contain ordinary pyogenic bacteria only, or these may be mixed with the Ducrey-Nuna bacillus of soft chancre, or it may contain no microörganisms whatever. In the last-mentioned instance, however, it must not be assumed that the suppuration is due to the absorption of toxins alone, as has been contended, but it is undoubtedly dependent upon specific bacilli which have succumbed shortly after entering the gland. Buboes from urethritis are not nearly so common as those from soft chancre and they rarely, if ever, contain gonococci.

Glandular tuberculosis is sometimes responsible for an abscess in the groin, as is also excessive walking, such as is imposed upon soldiers during a forced march. Climatic and other obscure causes are at times in evidence, and König even mentions "epidemics." Bubonic plague is a well-known cause.

Syphilitic buboes seldom suppurate, and when they do it can be assumed that a mixed infection exists.

Course and Symptoms.—Soreness and stiffness in the groin are rapidly followed by perceptible swelling of the lymph nodes, accompanied in most instances by more or less pain, which may suddenly cease upon glandular rupture. The glands, especially the superficial ones, are at first readily outlined and perhaps movable; but later periadenitis develops, the skin participates in the inflammatory process, and a brawny, dusky-red, or bluish swelling results in which the individual glands are lost. Infection may confine itself to one gland, or the entire inguinal packet can become involved.

In most instances suppuration occurs early, extends rapidly, and is easily detected through softening and fluctuation; but in other cases it is delayed and develops with extreme slowness, this being especially characteristic of the larger and harder swellings involving many glands.

In connection with the deeper glands, pus may burrow extensively beneath the fascia, between the muscles, and along the vessels, leading to the formation of troublesome sinuses. Rosenmüller's gland, lying within the femoral ring, is especially prone to give rise to such complications.

The degree of fever and other general disturbance varies with the character of the local inflammation and its acuteness. Chronic cases, with wide-spread induration, may cause no general reaction whatever, while an apparently insignificant acute adenitis can give rise to extreme pain, high fever, rapid pulse, and other marked and annoying symptoms.

Resolution may take place at any time, even after pus has formed and softening is evident, although this is rare. As a rule, after the development of periadenitis it is useless to look for spontaneous retrogression.

In so-called *chancroidal* or *virulent buboes* arising from soft chancres, phagedenic ulcers may develop in the groin following incision or spontaneous rupture. Even when phagedena is absent, periglandular inflammation is apt to be more marked and the edges of the skin undermined and ragged in appearance. In the depths of such an unhealthy ulcer may often be seen the remnants of infected glands.

Treatment.—Prophylaxis is of importance, as it cannot be doubted that early and proper attention given to lesions of the lower extremities and genitalia will prevent the development of inguinal infection. This accounts for the greater frequency of buboes in hospital than in private practice. Even after adenitis has appeared, much can be accomplished by prompt treatment of the local sore; in fact, this may be all that is required. It is better, however, to apply certain local measures, such as an ice-bag, hot fomentations, tincture of iodin, ichthyol, blue ointment, etc. Rest of the part is of course desirable, and moderate pressure is often of use. The latter is obtained by the application of a suitable bandage over a compress, or a bag of shot or other weight (two to four pounds), which may be heated. A hot-water bag is useful.

After suppuration has occurred, even when softening and fluctuation are present, retrogression may still take place if the process is confined within the capsule of a gland, although this is seldom the case. It is usually necessary to open and drain the focus, or adopt one of the various "abortive" forms of treatment. If the former method is chosen, the incision should be large enough to secure free drainage, which sometimes requires a small opening and sometimes a large one, no general rule being applicable to all cases. The cut should in one instance be parallel to Poupart's ligament, and in another vertical to the axis of the thigh, according to the judgment of the operator, remembering that vertical incisions are apt to stay open better than longitudinal ones, especially when the thigh is flexed. Remnants of glandular tissue which have failed to disintegrate should be cautiously removed with the curette. Violent scraping has been known to cause septic absorption and even pyemia.

It is probably not true, as contended by Strauss and others, that chancroidal infection never takes place through the lymphatics, but is always conveyed externally by contamination from the original sore. Nevertheless, it is well to use every precaution against secondary inoculation, both at the time of operating and later, by means of carefully arranged dressings.

Abortive treatment is especially applicable when the infection is confined to a single gland, and is employed both before and after pus has appeared, opinions differing widely as to its effectiveness. There can be no question that success often follows its use, although many of the brilliant results have undoubtedly been due to natural retrogression of the trouble. Several procedures may be mentioned:

Lang's Method.—After evacuating the pus through one or two small incisions, or by aspiration, the cavity is distended, by means of a hypodermic syringe, with a 1 per cent. solution of nitrate-of-silver, which is carefully massaged into all recesses. This is repeated every second day until the discharge becomes watery, when the injections are stopped and pressure is applied.

The Method of Welander and Spietschka.—The pus is aspirated and replaced with a 1 per cent. solution of hydrargyrum benzoicum oxydatum. The injection (ten to fifteen drops) may even be made into the unsoftened gland itself for the purpose of killing germs or hastening the process of disintegration. Occasionally suppuration is entirely prevented. Ten to twenty minims of a 3 per cent. solution of carbolic acid has been similarly employed.

Hahn's Method.—This consists in aspiration and irrigation with a 0.6 per cent. solution of salicylic acid until the fluid returns clear. If it is necessary to repeat the washings, normal salt solution is used instead of the acid. Wölsch, however, claims almost equally good results with the salt solution alone.

Bichlorid of mercury (1 : 20,000), iodoform in oil or in vaselin, turpentine, and various other antiseptics have also been similarly used.

When periglandular inflammation once appears with involvement of the skin, or when numerous glands are affected, a more extensive operation is difficult to avoid. This may consist in free incision with curetting and drainage, or in complete removal of the involved lymph nodes. If the former course is adopted, it is often better to delay than to incise too early, in order to permit of more extensive softening, thus avoiding the formation of obstinate sinuses leading to incompletely broken-down glands, which may persist for many weeks or even months. If sinuses already exist, they must be followed to their terminations and all gland tissue removed, which is often difficult, as the tortuous channels may ramify widely beneath the deep fascia.

Multiple glandular involvement, especially when the packet is indurated, may call for extensive dissection in order to remove all infected tissue and cut short the disease. The incision should be ample, the drainage effective, and great care must be used not to injure the femoral vessels, which should be accurately located beforehand, if possible. It must not be overlooked that such operations occasionally lead, when all the lymphatics are removed, to chronic edema of the lower extremity or genitals, at times so marked as to resemble elephantiasis. Fortunately, this is rare.

These larger operations are difficult and should not be undertaken hastily or in all cases. Early operation is, however, justifiable when the deep glands are involved, especially that of Rosenmüller in the femoral opening, or where the saving of time is an object.

Lennander has perfected a procedure for the *removal of all the inguinal glands*, including those within the pelvis as far as the bifurcation of the aorta. It is particularly applicable to malignancy and tuberculosis, although it may be briefly mentioned here. An incision is carried from the symphysis pubis to the anterior superior spinous process of the ilium and along the crest of that bone for half its length. After dividing Poupart's ligament at its inner extremity, the peritoneum, together with its contents, is retracted upward, thus freely exposing the field of operation. A second incision may be vertically extended down the thigh as far as necessary. Careful reunion of Poupart's ligament insures firmness of the scar.

Abscess of the Popliteal Space.—The popliteal space, lying posterior to the knee-joint, is covered by a firm fascia, connecting with that of the thigh above and the calf of the leg below. Together with vessels and veins it contains four small lymph nodes, lying in the center line, and several more or less constant bursæ situated laterally, which often communicate with the joint.

The principal *causes* of popliteal abscesses are inflammation of glands or bursæ, traumatism, inflammation of varicose veins, osteomyelitis of the lower end of the femur or upper end of the tibia, suppurating aneurism, and tuberculosis or syphilis.

The *symptoms* may at first be obscure and consist of pain only, together with a tendency to flex the knee. Later, a more or less brawny, red, tense, and tender swelling appears. Owing to pressure on vessels and lymphatics, the entire leg below the knee may become edematous. Pain is usually prominent, and constitutional disturbances may be profound in acute cases, consisting of high temperature, rapid pulse, and marked cerebral symptoms. Pus may spread beneath the deep fascia up into the thigh or down into the leg, or the knee-joint may become infected, either directly by lymphatic absorption or through the medium of an inflamed bursa.

Involvement of the lymph nodes is fortunately not common, although it occasionally arises in connection with inflammations about the feet or calf of the leg. In the beginning, before they are obscured by exudation, the movable glands can sometimes be felt in the central line of the popliteal space. Inflamed bursæ are situated more laterally.

Osteomyelitis is a sufficiently frequent cause to be always borne in mind. The original swelling may subside, to reappear later, the secondary trouble being due to the presence of a flake of necrotic bone. The inflammatory focus is so deeply seated that there may be almost no external manifestations for several days—simply intense pain, flexion of the joint, and pronounced constitutional symptoms.

Suppuration of an aneurism is rare. The diagnosis can usually be made from the history of a pulsating tumor combined with evidences of inflammation. The usual signs of aneurism, however, are lacking, and there is absence of pulsation in the vessels below, and swelling of the leg;

but it must be remembered that these symptoms can arise from pressure exerted by a deep abscess alone.

Tuberculous abscesses may originate in the joint, in the bones, or in the popliteal glands; or they may gravitate from above—even from such remote regions as the pelvis or spine. When this is the case they follow the large vessels or the great sciatic nerve.

As complications, may be mentioned involvement of the knee-joint (most common in bursal inflammations), thrombosis of veins and pyemia, ulceration into the popliteal artery and hemorrhage, the formation of sinuses (kept up by thick abscess-walls and movement of the part), and cicatricial contraction resulting in flexure and even ankylosis of the joint.

Treatment.—A free opening should be made at the earliest possible moment after the formation of pus, and efficient drainage instituted. When there is reason to anticipate embarrassing cicatricial contraction, it should be guarded against by early skin-grafting or the application of flaps from the same or the opposite limb. In the case of an old sinus, careful examination should be made for the presence of dead bone, which is often difficult to locate. If this is absent, rest of the part and cauterization will generally effect a cure, provided a suppurating bursa is not responsible for the difficulty, when an extensive dissection may be required.

A suppurating aneurism must be opened and drained like any other abscess; but immediate or subsequent amputation may be required. Tuberculous abscesses must be handled according to principles laid down elsewhere.

Cold Abscess.—Tuberculous abscesses are frequently known as "cold," "scrofulous," "chronic," or "lymphatic." Strictly speaking, they are not abscesses at all, but merely collections of liquefied tuberculous material, although macroscopically their contents so closely resemble true pus that it is difficult or impossible to distinguish between them, unless they happen to contain masses of caseous material or their course and history have been carefully ascertained. Microscopically, this "tuberculous emulsion" contains but comparatively few leukocytes, together with much fatty and granular detritus. Tubercle bacilli are rare and hard to find, and if the diagnosis depended upon their demonstration the surgeon would often be left in doubt. They are most numerous in the abscess wall. Even when they cannot be discovered with the microscope, however, inoculations of animals give positive results.

Cold abscesses usually arise in the young, from tuberculous lymph nodes or from diseased bones or joints, and they may contain fragments of bone, or masses of caseous material. The contents may be thick and creamy, like ordinary pus, or watery and "curdy." Although the abscess-cavity is lined with a more or less definite layer of tissue, containing tubercles—the so-called "pyogenic membrane," or "prophylactic membrane," according to Park—it is not definitely walled off with indurated inflammatory embryonic tissue, as in simple suppuration. Neither is the skin involved, unless the process has approached very near the surface, and then it is not red and infiltrated but thin, livid, and tuberculous.

Scrofulous abscesses sometimes become enormously large. They have a strong tendency to "gravitate" in the direction of least resistance —from the lumbar vertebræ, for instance, along the psoas muscle to the groin and sometimes to the thigh.

Various pathogenic microörganisms, including those which form pus, will grow luxuriantly in this tuberculous material, so that mixed infections, which are not uncommon, especially immediately succeeding the opening of a cold abscess, may give rise to very serious disturbances both local and general. The chills, sweats, and high, irregular temperature form what is known as "hectic fever," which is accompanied by emaciation.

The *general symptoms* of purely tuberculous abscesses vary much according to the resisting powers of the individual, but they do not resemble very closely those of ordinary suppuration. A slight evening rise in temperature is nearly always present, together with a subnormal temperature in the morning. Although loss of flesh and strength and the appearance of anemia are the rule, they may not occur unless mixed infection takes place. There is no leukocytosis. Amyloid (albuminoid) degeneration may appear in the course of time.

The *local symptoms* are also surprisingly mild; often depending more upon pressure on organs and nerves than upon activity in the process itself, so that large fluctuating abscesses may exist in various parts of the body, even about joints, with but little inconvenience to the patient. Unless the purulent collection be extremely near the surface, the skin remains whitened or unchanged, a phenomenon which has given rise to the name "white swelling" in tuberculosis of the knee.

Diagnosis is based upon the extreme chronicity of the process, combined with the history of tuberculosis in the individual or in the family; upon the absence of the signs of ordinary suppuration; and upon the presence of various pressure symptoms. The careful use of a sterile aspirating needle is often of great service in clearing up obscure cases. Tuberculin may be employed with caution.

Treatment varies much according to circumstances. The rule applying to ordinary suppuration, that wherever pus exists it must be evacuated at once, does not hold good in tuberculous conditions, unless mixed infection is present. It is often preferable to let the abscess alone, placing the part at rest and the patient under the best possible hygienic conditions, and patiently await absorption, which will occur in time in a fair number of instances.

In other cases aseptic aspiration may be resorted to, followed by irrigation with normal salt solution or some antiseptic, and the insertion of varying amounts, perhaps several drams, of a sterilized 10 per cent. suspension of iodoform in olive oil or glycerin. Occasionally, other fluids may be used; for instance, camphorated naphthol.

Again, it may be best to incise the abscess, scrape and wash out the contents, and drain under an aseptic dressing, guarding as carefully as possible against secondary infection, especially during the first few days. This method is particularly called for when pressure-symptoms are prominent or when spontaneous rupture is imminent. It cannot be employed in connection with joints with as much safety as elsewhere.

Bier treats tuberculous abscesses by sucking out the contents through small incisions by means of glass "cups" in which a gentle vacuum is produced through the action of a rubber bulb. (See Treatment of Acute Abscess, Fig. 57.) Not only is the purulent material thus removed, but a local hyperemia is produced, which Bier regards as highly beneficial in all tuberculous lesions. The process is employed once daily during a sitting of three-quarters of an hour, the bulb being kept in place about three minutes and then removed for five minutes, in order to avoid discomfort or too strong suction upon the tissues. Care must be used not to produce secondary infection of the abscess. It is well, when an extremity is involved, to combine this vacuum-treatment with the production of passive venous hyperemia by means of elastic constriction. This is obtained by applying a thin, Martin's rubber-bandage in several layers about the thigh or the upper arm, as the case may be, just tight enough to produce marked venous congestion *without causing pain, swelling, coldness of the part, or interference with the arterial circulation as judged by the pulse.* (See Treatment of Acute Abscess, Fig. 59.) The bandage should be left in place two, or at most three, hours daily, and the treatment should be begun as early as possible after the appearance of the abscess. It is applicable to old and young alike, and is used even in the presence of ulcerations and fistulæ. Splints are unnecessary, and the treatment is often left in the hands of the patient. Brilliant results are claimed by Bier, which have been substantiated in part by others.

Iodoform injections are never used by Bier except when a joint like the knee is distended with serous or purulent fluid, and even then they are always followed by the production of artificial venous hyperemia, upon which the greater dependence for an ultimate cure is placed.

Cold Abscesses in Different Regions.—*Retropharyngeal Abscess.*—This generally arises from caries of the upper cervical vertebræ, although it may have its origin in the prevertebral lymph nodes or in the bones of the base of the skull. It bulges forward the posterior wall of the pharynx, where it may be seen and felt, and is apt to cause difficulties in deglutition and respiration.

Early incision may prevent burrowing into the posterior mediastinum or suffocation from bursting into the larynx. The opening must be made from the side of the neck posterior to the sternomastoid muscle rather than through the mouth, in order to keep pus out of the air-passages and to avoid secondary infection and sepsis.

Tuberculous abscesses of the neck, often designated as "scrofulous," frequently arise from lymph nodes which receive their infection in most instances from the tonsils, teeth, or ears. They are seldom large, and they have a tendency to break through the previously involved skin, leaving puckered and disfiguring scars. They are treated by aspiration and injection of iodoform, camphorated naphthol, etc., by excision, or by incision, curettement, and drainage, combined perhaps with suction by means of a vacuum-cup, according to Bier.

Mediastinal Abscesses.—Tuberculous collections of pus in this region arise from diseases of bone, glands, pleura, etc., or they descend from the neck above. The diagnosis is difficult unless pointing has occurred or the presence of bone-involvement throws light upon the condition. Pressure-symptoms and the history of the case are significant, and the X-ray and exploratory punctures may be of material assistance. Early incision and effective drainage are indicated.

Abscesses of the Ribs.—Purulent foci surrounding a tuberculous rib are not uncommon. The history will prevent their being confused with typhoid abscesses, which they closely resemble. Excision of the diseased section of the rib is usually required, and even then relapses are not infrequent.

Psoas Abscesses.—These have their origin in the bodies of the dorsal or lumbar vertebræ, where some irregularity of the spine can usually be detected. They gravitate along the course of the psoas muscle to the groin, where they point below Poupart's ligament externally to the great vessels. They sometimes contain large quantities of pus and fragments of bone. They may be treated by aspiration, irrigation, and injection of iodoform suspended in oil or glycerin, by aseptic incision and drainage, or by the Bier vacuum method. Support and fixation of the spine are indicated.

Other chronic abscesses presenting in the same region may be glandular, or they may arise from disease of the sacrum, pelvis, or lower lumbar vertebræ, the pus finding its way around beneath the iliacus muscle.

Tuberculous abscesses of the hip develop during the course of coxitis and are the cause of the sinuses so frequently met with in the later stages of this disease. Prolonged hectic fever following rupture and secondary infection, succeeded perhaps by amyloid degeneration of various organs, is a frequent cause of death. The injection-treatment generally fails in this location, and incision must often be combined with resection of the diseased bone before a cure is obtained. Fixation and extension are valuable aids to treatment.

Tuberculous abscess of the knee is a frequent accompaniment of so-called "white swelling" of the joint. It may be peri-articular or articular, osseous or capsular in origin. If the bones are not too extensively involved, aspiration followed by injection of iodoform occasionally affords relief, but usually resection of the joint, or at least an arthrectomy, is called for. A plaster cast or an appropriate brace is of material aid in securing absorption. In extensive tuberculosis of the joints of the lower extremity, especially in working-people no longer young, amputation is always to be considered. Passive venous congestion produced by the Bier method of elastic constriction often gives good results, although it is less effective with the knee than elsewhere.

Cold abscesses of the wrist, ankle, elbow, and shoulder require immobilization of the joints, with the addition, perhaps, of injections of iodoform, incision, arthrectomy, or excision, according to circumstances. The treatment by venous congestion is worthy of consideration.

Tuberculous abscesses of the long bones nearly always occur in the epiphyses rather than the diaphyses, the head of the tibia being a favorite site (Brodie's abscess). In the fingers, however, a purulent collection sometimes surrounds the diaphysis of one of the phalanges, giving rise to what is known as *spina ventosa.*

The *breast, prostate, epididymis, ischiorectal fossa,* and *kidney* are frequently the seat of tuberculous suppurations, while in the *brain, mammary gland, suprarenal capsule, liver,* and other organs they occur less frequently.

III. FISTULA AND SINUS.

Definition.—The terms fistula and sinus are used somewhat interchangeably, although each has its own application. *Fistulæ* refer more particularly to abnormal openings of some permanency between normal cavities or canals, or between such cavities and the surface of the body, such as from the rectum to the bladder, from the urethra to the vagina, or from the rectum to the skin surrounding the anus. The word *sinus* is generally used to designate a more or less persistent suppurating tubular tract in the tissues, with but slight tendency to heal, such as is left after the spontaneous opening of an abscess. It is often long, narrow, and tortuous. A small ulcer, if it extended deeply enough to form a granulating channel, would become a sinus; and, conversely, if a sinus should heal almost to the surface, it would become an ulcer. Sinuses and fistulæ, especially the former, are usually, but not always, lined with granulations, and they are often surrounded by walls of fibrous tissue, sometimes of considerable thickness, which are an expression of long-continued irritation and an effort at repair.

Fistulæ are designated according to the regions in which they are found, the cavities or organs with which they communicate, or the material which passes through them; for instance, *perineal fistula, gastric fistula, prostatic fistula, vesicovaginal fistula, rectovaginal fistula, fecal fistula, biliary fistula, urinary fistula, salivary fistula,* and *aërial fistula,* etc. The last named refers to fistulæ communicating with the air-passages, particularly with the trachea and larynx. An opening joining two cavities lined with mucous membrane, such as two coils of intestine, is sometimes called a *bimucous fistula.*

Causes.—(1) Some fistulæ are congenital, and arise from imperfect closure of a branchial cleft in the neck, of the urachus, or of the omphalomesenteric duct.

(2) Sinuses may arise from abscesses discharging themselves through openings which refuse to close because they are too narrow or too obstructed to admit of perfect drainage, or because there is too much movement in the surrounding tissues to permit of necessary rest of the part. Such movement may be due to the action of a muscle, for instance, the sphincter ani in anal fistula, or the movements of respiration, as is some-

times the case in sinus or fistula of the loin following perinephritic suppuration.

(3) The presence of foreign bodies or necrotic tissue, such as dead bone, bullets, ligatures, fecal concretions in appendical abscesses, sloughing tendons, etc., may determine the existence of a sinus.

(4) Inability of a pus-cavity to collapse owing to rigidity of its walls may cause sinus or fistula, as in empyema of the thorax or antrum, or an old cavity in the lung.

(5) The presence of some specific germ, such as exists in tuberculosis or syphilis, is so frequently a cause of sinus that tuberculosis at least should be suspected in every case the origin of which is not otherwise easily explained.

(6) The sloughing of tissues, such as occurs about the vagina in childbirth or the mouth in noma, may cause rectovaginal or vesicovaginal fistulæ, or give rise to a fistula through the cheek.

After a fistula has formed it may be kept up, in spite of the disappearance of the original cause. by the passage through it of substances irritating or otherwise, such as fecal matter, urine, or saliva.

Diagnosis.—This is usually easy. An opening is observed, often retracted below the level of the tissues, into which a probe may be passed, and from which issues pus, air, gas, or some secretion or excretion. Occasionally, however, the mouth of a sinus or fistula is obscured by exuberant granulations, especially if a foreign body is present, such as dead bone. Some sinuses even have a tendency to become closed temporarily by a thin pellicle of epithelium, which renders their detection difficult, though if the right place be touched, the probe will readily break through.

Treatment.—As most fistulæ depend upon local difficulties, constitutional treatment is of little avail, except in tuberculosis and syphilis, where it is often of the greatest service. It is worthy of note, however, that during the course of some intercurrent disease, such as erysipelas, fistulæ sometimes disappear.

The first and most important consideration is the removal, if possible, of the cause. Foreign bodies should be extracted, which may necessitate the chiseling away of dead bone; and drainage must be improved, which often means counter-openings or the widening of the original channel, combined with gauze packing, with the view of encouraging healing from the bottom.

Sinuses often form in connection with non-absorbable ligatures or sutures, especially silk, and persist until the offending substance is removed, which may require an extensive operation. Often, however, such sutures can be fished out with a small blunt hook. Or a few strands of silkworm-gut may be bent into a loop, bound to the end of a probe, inserted in the sinus, and twisted about until the suture is entangled and extracted.

When a sinus leads through a serous cavity, or is near an important structure such as a large vessel, great care must be used in widening it with a knife, as peritonitis, pleurisy, or hemorrhage have often been caused in this way. In such cases it may be better to dilate rapidly with forceps, or slowly with rubber tubes.

Rest is sometimes so important a factor in the cure that the division of a muscle is indicated in order to obtain it—for instance, the sphincter muscle in anal fistula. In other cases rest can be secured by the use of splints, as in sinuses about the popliteal space.

A thoracic fistula, when depending upon an old empyema, may necessitate the extensive removal of ribs, according to Estlander, or even of the entire chest wall, as recommended by Schede, in order to permit of collapse of the cavity.

In treating sinuses which ramify beneath the skin, it is frequently necessary to split them up extensively, as is so often done in the vicinity of the anus, thus converting them into open wounds which can be scraped and packed with gauze. Especial attention should be given to pockets of pus.

If a sinus has its origin above or behind a stricture of the bowel or urethra, it is necessary to treat the stricture before the sinus will heal. The same principle applies in other regions; for instance, a biliary fistula of the gall-bladder may not close until a stone is removed from the common duct, and a urinary fistula of the kidney will not disappear until an obstruction of the ureter is cleared away.

In some cases quite simple means are sufficient, such as thorough scraping with a small sharp spoon, burning with the electrocautery, which is very effective, especially in urinary fistula; or the use of some chemical cauterizing agent, such as pure carbolic acid, zinc chlorid, tincture of iodin, silver nitrate, etc. Carbolic acid is best applied on cotton wrapped tightly about a probe, with a bulbous end to prevent the cotton slipping off, and silver nitrate can be fused onto the same instrument. The milder antiseptic solutions are of less service. Hydrogen peroxid may do harm by sudden gaseous expansion, especially about the mouth and neck.

Sometimes a sinus or fistula may be dissected out bodily with advantage. The method is frequently resorted to in fecal fistulæ of the intestines, primary union being often obtained.

Fistulæ about the vagina, mouth, urethra, and elsewhere often require more or less complicated plastic operations, which sometimes tax the ingenuity of the surgeon to the utmost. It is in such cases that the injection of paraffin into the surrounding tissues, according to Gersuny, is of great advantage, although the danger of embolism must not be overlooked. For this purpose any strong aspirating syringe may be employed, but it should have a metal piston so as to permit of absolute sterilization by boiling. Rather a large needle is necessary. Sterile paraffin with a melting-point of from 103° to 110° F., obtained by adding an appropriate quantity of white vaselin, is probably the most desirable, because it can be solidified in the syringe and pushed through the needle into the tissues in this condition, especially if the syringe be constructed so as to permit the application of considerable force to the piston. Paraffin with a melting-point of from 140° to 160° F. is also used. It is injected while hot and in a fluid condition and allowed to solidify within the tissues. Fluid material, however, is harder to manage than solid, owing to too rapid cooling and uncontrollable diffusion in the cellular tissues. There is also more danger of embolism and of necrosis from too high a temperature.

The paraffin soon becomes surrounded by fibrous tissue which penetrates it in every direction, converting it into a cartilaginous-like mass, which may effectually close the fistula.

Tuberculous sinuses are troublesome because of their refusal to heal until all infective material has been removed, and sometimes this is impossible even though the most serious and extensive operations are resorted to. As instances may be cited spinal caries, hip disease, and white swelling of the knee.

Fistulæ in Different Regions.— **Salivary fistula** usually arises from a break in the continuity of Steno's duct, although it may be caused by wounds or abscesses of the parotid gland. The former condition is difficult to cure and usually requires one or more operations, while the latter often recovers spontaneously or can be obliterated by cauterization, especially with the actual cautery. Any opening into the mouth or pharynx may give exit to more or less saliva, but it is not strictly a salivary fistula.

Branchial fistulæ are found in the neck and occasionally in the lips or cheek, although rare in any situation. They arise from imperfect closure of the branchial clefts. They may be complete or present an opening upon the cutaneous or mucous surface only ("blind external" and "blind internal" fistulæ, Fig. 62). The external opening is generally near the anterior border of the sternomastoid muscle, while the internal is in the floor of the mouth, often in or near the tonsil. They are lined with epithelium and secrete a watery fluid.

Treatment is not always necessary; but when required, it consists in cauterization, incision and packing with gauze, or extirpation, the last frequently requiring extensive and difficult dissections.

Thyroglossal Fistulæ. (See Surgery of the Neck.)

Gastric fistulæ seldom arise spontaneously, but are usually due to surgical intervention, as in stricture of the esophagus. Unless carefully guarded against, by protective salves, constant cleanliness, etc., extensive erosion of the skin is apt to occur from the corroding action of the secretions of the stomach. These fistulæ have a strong tendency to close spontaneously and must be kept open by tubes when this is desired. In order to close them the abdomen must be opened and the aperture in the stomach obliterated by a suitable operation.

Fecal or intestinal fistulæ are openings leading into any portion of the bowel except the lower part of the rectum, where they are known as rectal or anal fistulæ. The term fecal, however, applies to those fistulæ only through which the contents of the bowel find exit. Fecal fistulæ are often erroneously supposed to exist in connection with abscesses near the bowel which contain colon bacilli, for instance, in appendicitis, on account of the foul odor, this being particularly true when gauze packing has been employed. Every fecal fistula has a strong tendency to spontaneous closure, including those complicating operations for appendicitis, although they sometimes require cauterization or extirpation.

Biliary fistulæ exist in connection with the gall-bladder or bile-ducts, either within the liver or after leaving it. In the vast majority of instances their persistence indicates some obstruction, such as stone or stricture, in the duct beyond. In the case of the gall-bladder itself, if the obstruction is in the cystic duct the discharge from the fistula will be mucus and not bile.

Treatment consists in cholecystectomy or removal of the obstruction in the ducts, according to circumstances; or in making a new fistulous opening between the gall-bladder or the common or hepatic duct, and some portion of the intestinal tract, so as to secure internal drainage.

Anal or rectal fistulæ occur in connection with the lower extremity of the rectum and have little tendency to spontaneous cure. They are usually complete, but they may have a cutaneous or a mucous opening only—*incomplete or "blind" internal or external fistulæ* (Fig. 62). Fecal matter, gas, or pus only may pass through them. They usually arise from the rupture of ischiorectal abscesses and are often tuberculous. (See ischiorectal abscess.) A "horseshoe fistula" is one which has dissected around the bowel, with an opening into it upon either side as well as externally.

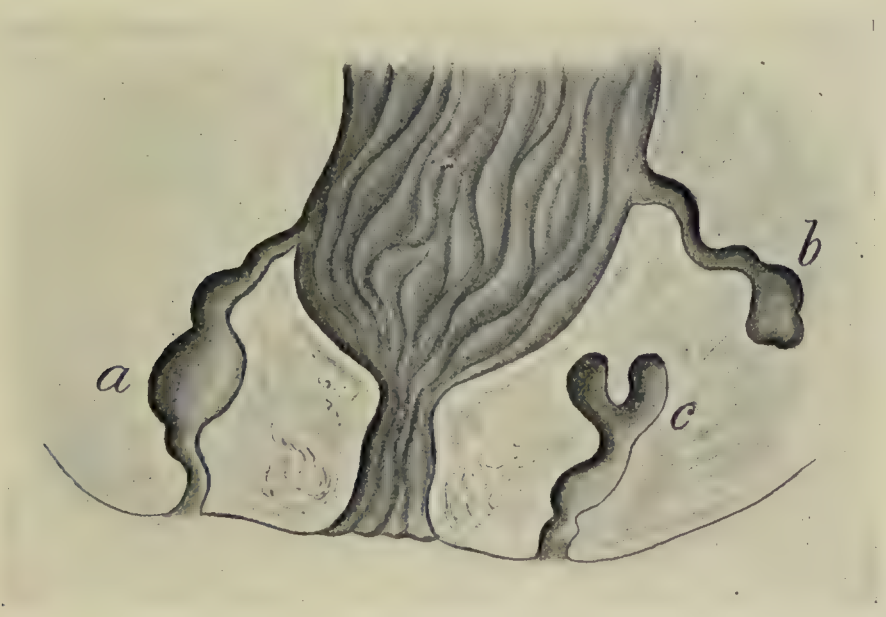


FIG. 62.—DIAGRAM OF ANAL FISTULÆ.
a, Complete; *b*, blind internal; *c*, blind external (modified from Duplay and Reclus).

The accepted mode of *treatment* is to slit up the fistula so as completely to divide the sphincter muscle, in not more than one place, however, for fear of permanent paralysis. The wound should be packed with gauze. Rest is thus obtained for the part together with healing by granulation from the bottom of the wound. Mere cauterization usually fails. Ligatures of silk or rubber, threaded through the fistula into the bowel and out through the anus and tied tightly over the skin, were formerly much more frequently employed than now. Tuberculous fistulæ require special consideration. They should not be operated upon hastily. (See chapter on Diseases of Rectum and Anus.)

Urinary fistulæ are often *perineal* or *penile*, but they may exist in connection with the ureter, kidney or bladder (vesical). They can occur from spontaneous rupture of the urethra behind an old stricture, or follow operations upon any portion of the urinary tract. They are frequently extremely difficult to heal, especially if some obstruction such as a stone or stricture exist in front of them. Cauterization (best with the actual cautery), plastic operations, prostatectomy, urethrotomy, and even removal of a kidney may be required.

Rectovaginal and vesicovaginal fistulæ may follow childbirth or be caused by rectal or uterine carcinomata. The non-malignant forms sometimes close spontaneously, but they usually call for plastic operations which are at times complicated and difficult.

Umbilical fistulæ are in most instances due to a patent urachus or omphalo-mesenteric duct, although they may be intestinal or even biliary. Their treatment must be by cauterization or operation as circumstances may direct.

Bone fistulæ arise from carious or necrotic processes and require the removal of the diseased osseous structure before healing can be obtained.

Thoracic fistulæ have their origin in most instances in an old empyema, although sinuses from diseased ribs or abscesses of the breast are not uncommon. Very extensive resections of ribs (Estlander), or even the removal of the entire chest wall (Schede) may be called for, accompanied in some instances by decortication of the lung itself (Fowler).

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CHAPTER VII.

ULCERATION AND ULCERS.

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An ulcer is a superficial, granulating, infected sore, usually upon the skin or mucous membrane, with little or no tendency to heal. It may be looked upon as a chronic abscess from which the covering tissues are absent.

Ulceration is the process by which ulcers are produced and maintained. It is a form of chronic inflammation in which the reparative power is overshadowed or at least equaled by the tendency to destruction. As in an abscess, the tissues melt away into pus and granular detritus; but instead of the fluid remaining confined in a cavity, it is discharged upon a granulating surface, whence it quickly escapes. Gangrene and sloughing differ from ulceration in that they result in the death of large enough portions of tissue to be seen and handled; but this does not exclude the fact that these forms of tissue-death are practically the same and may all go on together, as, for instance, in a bed-sore. In this connection, an illustration may be drawn from the alluvial banks of a stream during high water—they may crumble slowly and almost imperceptibly away, as in ulceration, or they may cave in in great masses, as in sloughing or gangrene.

An ulcer is surrounded by a zone of inflammation, which often causes more or less infiltration with thickening and elevation of the tissues. In acute ulcers the exudate in this zone consists largely of polynuclear leukocytes, while in more chronic processes, proliferated connective-tissue cells and fibrous tissue predominate. Park regards the exudate from an ulcer as distinct from pus, and calls it *pyoid* or *puruloid* material; but in reality its relationship is so close that for all practical purposes it may be regarded as a variety of pus at least. In chronic ulcers, and those with a tendency to heal, fibroblasts are in preponderance and fibrous tissue appears, which, in ulcers of long standing, surrounds the sore on all sides and below with an indurated connective-tissue wall, the contraction of which cuts off the blood-supply, interferes with nutrition, and renders healing extremely difficult.

The surface of an ulcer is covered with "granulations," little elevations of cells around capillary loops, giving the roughness of a strawberry. Under favorable circumstances, these granulations are firm and red. When they are large and flabby, succulent and pale, or otherwise abnormal, it is a sign that the conditions are unfavorable, as is evidenced by the absence of a tendency to heal and a failure of efforts at the transplantation of skin.

An ulcerating area is often covered with a pellicle which sometimes approaches the character of a membrane and may conceal the granulations completely. It consists of exudative material and tissue débris and is usually a sign of defective vitality and reparative power. The cleaner and redder an ulcer is and the more easily it bleeds, other things being equal, the "healthier" it is.

Repair takes place through the agency of fibroblasts furnished by the connective-tissue cells. Near the open ulcer they form granulation-tissue (to be distinguished from "granulations") which gives place to fibrous tissue further away. In this manner the cavity gradually fills up to the level of the surrounding skin or mucous membrane. Then, from the edges, new epithelium spreads over the granulations in a whitish or bluish pellicle which has been likened to the reaching out of ice from the shores of a freezing pond.

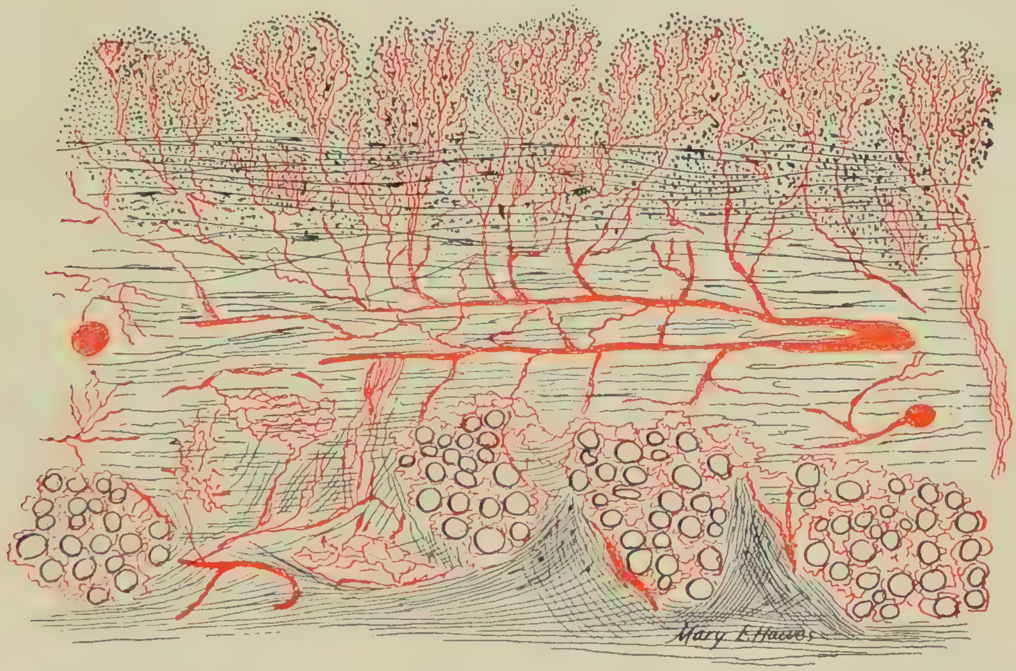

FIG. 63.—GRANULATION-TISSUE ON THE SURFACE OF AN ULCER; CAPILLARIES INJECTED WITH CARMINE.

When healing is complete the granulation-tissue has become scar-tissue; red at first, but turning more and more white as the numerous capillaries are interfered with by cicatricial contraction. In the majority of ulcers the contraction is of little moment, but in some situations it may cause deformity or interference with function, as, for instance, about the eyelids, lips, rectum, urethra, joints, etc.

Ulcers do not heal readily for a variety of reasons which center about a deficiency in general or local resisting powers. The patient may be diabetic, tuberculous, scorbutic, or syphilitic, or may have become debilitated from bad hygienic surroundings or from illness or injury. A local irritation may continue in such a way that healing becomes impossible; for instance, the rubbing of a shoe or some article of clothing, gall-stones in the biliary tract or fecal concretions in the appendix, the constant passage over the sore of fecal, urinary, or other discharges or secretions, lack of rest when the lesion is near a joint, etc. The circulation of the part may be poor, either from general causes, such as varicose veins of the leg, or more local reasons connected with the presence of excessive contracting scar-tissue which cuts off the blood-supply by the formation of a so-called "callous ring." More or less permanent damage to the vitality of the tissues may have been done by cold or heat or by such an agent as the Roentgen ray. Specific infections, such as glanders, anthrax, syphilis, or tuberculosis may be responsible.

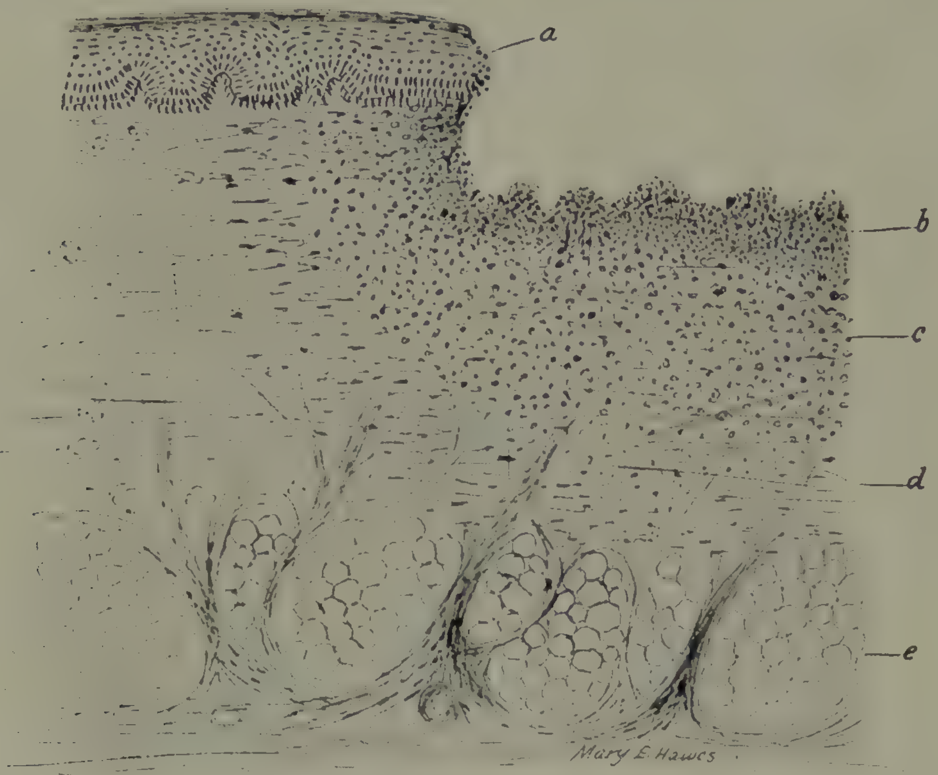

FIG. 64.—EDGE OF AN ULCER.
a, Epithelium; *b*, granulating surface; *c*, leukocytes; *d*, fibroblasts; *e*, adipose layer.

Occasionally patients will themselves mechanically irritate an ulcer so as to prevent healing, either because of hysteria, mental aberration, or a deliberate desire to defraud the observer.

CAUSES.

Ulcers are due to weak tissue-resistance, or to powerful external irritations, in which infection plays an important rôle; or frequently to a combination of these factors.

1. General Causes.—(*a*) Various devitalizing fevers and diseases, such as typhoid, diabetes, scorbutus, diphtheria, chronic nephritis, etc.

(*b*) Mineral poisoning, such as is produced by phosphorus.

(*c*) Anemic and debilitated conditions brought on by starvation, improper food, poor hygiene, overwork, dissipation, lack of sleep, etc.

2. Local Causes.—(*a*) Poor circulation and nutrition, such as is met with in connection with varicose veins of the leg; old scar-tissue, the contraction of which has cut off the circulation; continuous pressure, from splints, from lying in bed, etc.

(*b*) Poor innervation, as occurs when a nerve is divided, in bedsores due to injuries of the cord, and in various nervous diseases. In such cases the difficulty probably arises from lesions of vasomotor rather than "trophic" nerves, and from failure of the sensory nerves to give warning of impending trouble.

(*c*) Specific infection, as observed in tuberculosis, glanders, syphilis, chancroid, etc.

(*d*) Malignant disease, such as cancer, and sarcoma.

(*e*) Local destruction of the vitality of the tissues, as is produced by extremes of heat and cold, and sometimes by the X-ray or by radium, and by the poisons of reptiles or insects.

(*f*) Local irritation or injury of tissues; from violence, pressure or rubbing of clothing, or the presence of a foreign body, such as dead bone, a splinter, sloughing tendons, etc.

(*g*) Various diseases of the skin; for example, pemphigus.

In nearly all ulcers microörganisms are present, and they are more or less necessary to the continuation of the process. Without them it can hardly be called ulceration, but simply a granulating wound or surface.

Although any form of bacteria may find lodgment upon an open ulcer and perhaps grow there in profusion, the active agents are usually the staphylococcus and streptococcus pyogenes or the specific germs connected with such diseases as tuberculosis, syphilis, glanders, chancroid, typhoid fever, etc.

CLASSIFICATION OF ULCERS.

Ulcers are classified in various ways, giving rise to a multitude of terms, some in more or less general use and others obsolete; no hard and fast lines can be drawn, however, between the different kinds.

Healthy ulcers are those with active, red, firm granulations, secreting ordinary pus, and without too much tendency to resist the process of healing.

Indolent ulcers are those with pale, flabby, or edematous granulations, secreting watery or otherwise "abnormal" pus, and with an absence of activity either in the direction of healing or progression. Such sores are often surrounded by callous edges, or covered with a dirty membranous-like exudation, and are generally seen about the leg.

Irritable, painful, or erethistic ulcers are those which are more than usually painful, either spontaneously or when manipulated.

Hemorrhagic ulcers bleed easily, often without apparent cause.

Sloughing or gangrenous ulcers present sloughs of tissue upon their surfaces or around their edges.

Phagedenic ulcers extend rapidly by eating away the surrounding tissues. They may be sloughing, gangrenous, or hemorrhagic.

Fungous or fungoid ulcers show flabby and excessive granulations, rising above the surface and at times almost cauliflower-like. The term is often used, especially by the Germans, to indicate tuberculous ulceration.

The term *rodent ulcer* was formerly used to designate ulcers which "gnawed" deeply into the skin of the face. They are now known to be and are called epitheliomata.

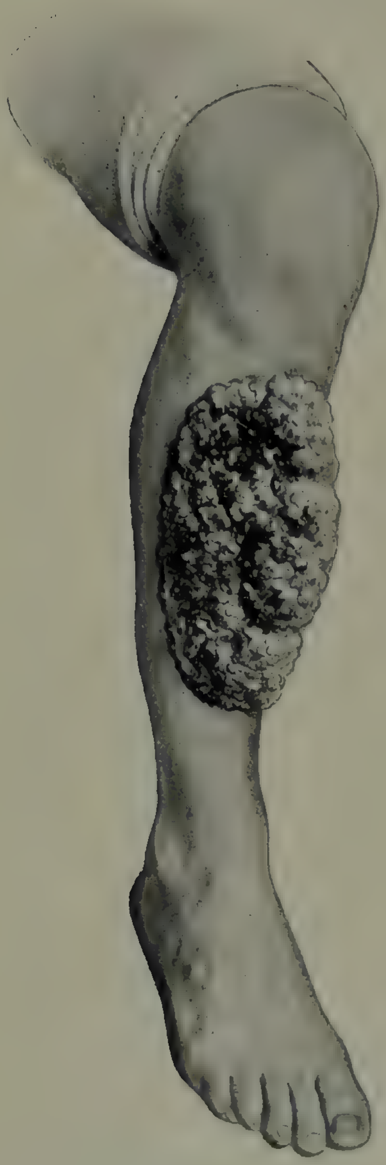

FIG. 65.—EPITHELIOMA FOLLOWING ULCER.

An *indurated ulcer* is one that is hard to the touch from fibrous tissue around its border and perhaps over its floor as well.

A *fissured ulcer* is one resembling a fissure in appearance, as in fissure of the anus.

A *fistulous ulcer* is one at the opening of a fistula.

When the border of an ulcer is spoken of as inflamed, edematous, livid, or tumid; or the surface as excavated, sloughing, or callous, the terms explain themselves, as do also those relating to size and shape of the sore and the character of the discharge. An *excavated ulcer*, for instance, refers to one which is considerably hollowed out, and a *serpiginous ulcer* to one which progresses from a common center more or less in segments of a circle.

Perhaps the most useful division of ulcers is into *Acute* and *Chronic*, although no sharp line can be drawn between them.

An *acute ulcer* is one which has formed or has a tendency to progress with comparative rapidity. There are about it none of the signs of chronicity, such as callous borders, pigmentation, indolent granulations, etc. Such ulcers often bleed easily, have undermined and ragged edges and irregular bases, and their surfaces may be covered with sloughs. A typical example is the typhoid ulcer of the intestines.

Chronic ulcers show signs of slow formation and progress. The surrounding skin is more or less indurated, thickened and even callous, and there is often a livid, brownish, or coffee-colored pigmentation. The floor of the ulcer, often adherent to the underlying structures, may be hardened by fibrous tissue. From this the "unhealthy" granulations may be scraped, leaving a firm whitish surface which bleeds but slightly owing to poverty of blood-vessels, which have been squeezed out of existence by cicatricial contraction. Poor circulation often causes the discharge to be more or less watery or gummy and with a tendency to form a membrane-like covering to the imperfect granulations. When the granulations are excessive and project above the surrounding surface, as they are apt to do in the presence of dead bone, they are commonly spoken of as "proud flesh."

Chronic ulcers, as well as the scars which they produce, sometimes form a basis for the development of epithelioma. This is known as *malignant degeneration* or *Marjolin's ulcer.* (For illustrations, see chapter on the skin, Vol. II.) The borders and base then become of a peculiar and striking thickness and hardness, as though the ulcer were embedded in cartilage, while the granulations feel firm and appear red and warty; the whole ulcer looks and feels hard and rough and bleeds easily. The corresponding lymph nodes are apt to become involved. This malignant change is sometimes seen in ulcers of the arms or legs and frequently occurs, it is believed, in ulcers of the stomach. The diagnosis can often be made in doubtful cases by microscopic examination of a small section. The treatment is by thorough extirpation or the use of the X-ray, rather than by cauterization, which often merely hastens the growth. In some cases amputation of a limb may properly be resorted to. In malignant degeneration of gastric ulcer early removal should be done, provided the diagnosis can be made.

VARIETIES OF ULCERS.

Varicose Ulcer is the most common form of *crural* or *leg ulcer.* It is found in connection with varicose veins, although not every case of enlarged veins is accompanied by an ulcer. The blood stagnates in the veins, and this leads to infiltration or chronic edema of the tissues, accompanied by poor nutrition and lessened resisting power. Damage to the lymphatics usually has more or less to do with the process also. Varicose veins arise from a variety of causes—from hereditary influences, dependency of the part, excessive walking and standing, the habit of crossing the limbs while sitting, childbirth, constipation, pelvic tumors, deficient innervation, femoral phlebitis, etc., heredity being probably the most important.

Even a trivial injury, such as a slight bruise, a scratch, or the rubbing of a shoe-top, may result in the breaking down of the poorly nourished tissues and the formation of an ulcer, which is always slow to heal. An eczema, due also to faulty circulation and nutrition or to irritating discharges, frequently accompanies the ulceration and often precedes it.

Age and sex are predisposing factors in varicose ulcers, they being more often found in women past middle life. The poor are afflicted most; which may be attributed to overwork, bad hygienic surroundings, uncleanliness, and neglect.

Through inflammation of a vein, or its rupture subcutaneously or externally, ulceration may be directly produced. Occasionally, such a rupture takes place in an old ulcer and a copious and perhaps dangerous hemorrhage results.

Varicose ulcers nearly always occur on the lower third of the leg or near the junction of the lower with the middle third. In cases which have existed for any length of time the skin presents evidences of poor nutrition, faulty circulation, and chronic inflammation. It is thickened, edematous, or indurated, and may pit on pressure. Pigmentation is nearly always present, the surface presenting a brownish, coppery, or bluish appearance. Subcutaneous ecchymoses are frequent, and the skin is often covered with eczematous crusts. Thickening and wartiness of the skin are sometimes so extreme as to result in a form of elephantiasis.

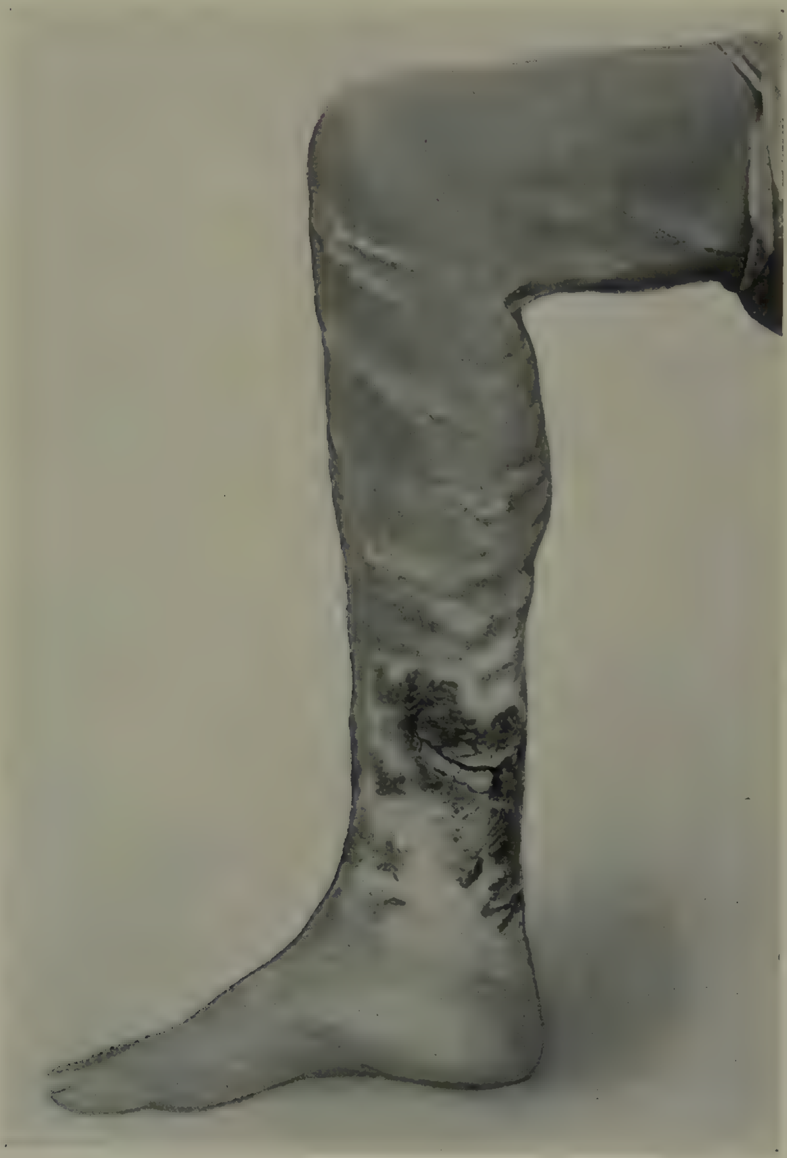

FIG. 66.—ECZEMA AFTER VARICOSE VEINS (FOX).

The sores themselves are generally single, although a number of small ulcers are often enough encountered in an area of diseased, livid, and almost necrotic skin, especially in the region just above the malleoli. These frequently coalesce later on. Occasionally very large ulcers are met with which almost or entirely encircle the limb and destroy most of the venous and lymphatic connections of the foot below, which swells accordingly; but generally the affected area is of moderate size and the foot is undisturbed.

The surfaces of varicose ulcers usually present imperfect and unhealthy granulations, secreting a more or less thin and offensive pus, and they are sometimes covered with membranous exudation. The edges and base are thickened and callous; and enlarged veins, capillary or otherwise, are present near the circumference and often amount to genuine blood-sinuses which tunnel the infiltrated tissues. In examining such an ulcer one gets the impression of a great pigmented scar, the center of which has broken down. Lymphangitis, erysipelas, and venous thrombosis are not of infrequent occurrence in connection with varicose ulcers, while embolism and even pyemia are sometimes met with.

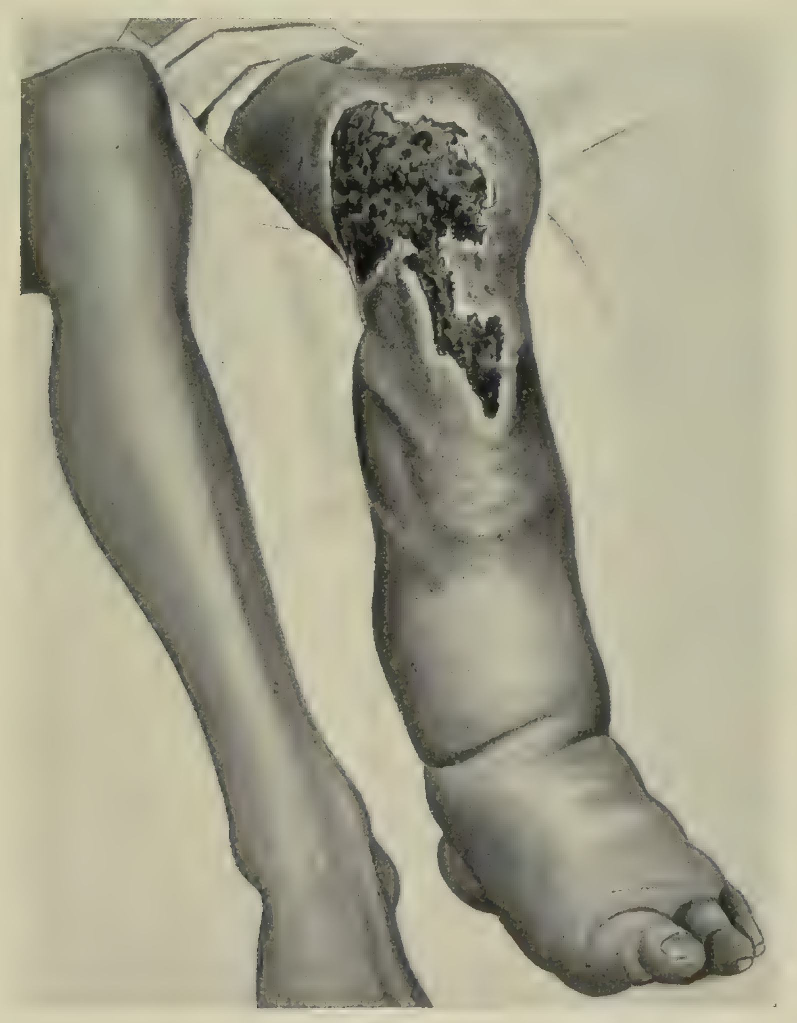

Fig. 67.—Ulcer Followed by Elephantiasis (König).

As extreme and unusual **complications** in bad cases should be mentioned necrosis of bone, the formation of osteophytes, involvement and ankylosis of the ankle-joint; together with atrophy and contracture of muscles and adhesions of tendons, perhaps giving rise to various deformities of the feet, such as flat-foot or even club-foot.

The **symptoms** of most leg-ulcers are not severe, although some ulcers are painful in the extreme. In the course of years individuals become in a great measure accustomed to the affliction and correspondingly neglectful of it. It is not uncommon, especially among the lower classes, to see an ulcerated leg enveloped in a disarranged, pus-soaked, foul-smelling bandage which has not been changed for days.

The **diagnosis** of varicose ulcers is usually easy; but the mere presence of enlarged veins, it should be noted, is not pathognomonic, because they may easily exist along with ulcers of other origins—tuberculous, syphilitic, neurotic, etc.

Syphilitic ulcers of the leg, from cutaneous or periosteal gummata, are not uncommon. They present an eaten-out appearance, with sharp edges, and generally lack the callous margins of the varicose type. They are more often multiple, and are apt to occur in the upper and middle thirds of the leg, especially about the calf. Quite characteristic coffee-colored pigmentation of the skin results. When the diagnosis is at all doubtful, specific treatment (potassium iodid internally and mercurial plaster locally) should always be vigorously employed.

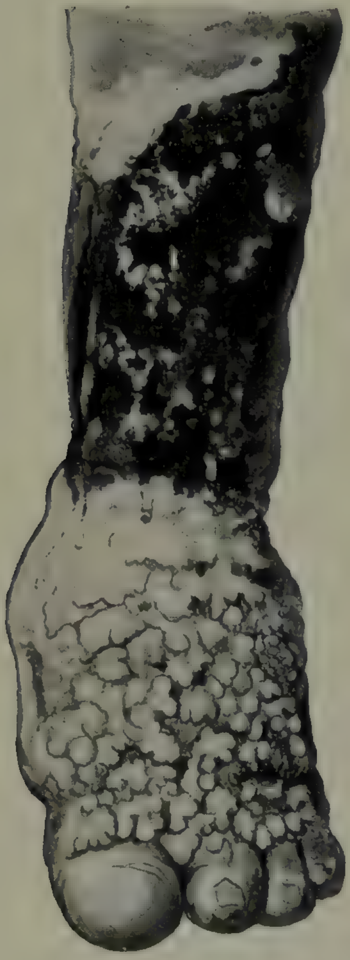

FIG. 68.—CIRCULAR ULCER OF THE LEG, WITH ELEPHANTIASIS OF THE FOOT (von Bruns).

The **treatment of varicose ulcers** must be based on (1) antiseptic cleanliness and (2) improvement of nutrition by betterment of the circulation of blood and lymph.

(1) *Cleanliness.*—In aggravated ulcers, especially those accompanied by old crusts, ill-smelling discharges, and various inflammatory conditions, the leg should be washed once or twice daily with suds and a piece of gauze and shaved when necessary. Warm fomentations should be employed, such as boric acid, acetate of lead, acetate of aluminum, etc., the stronger antiseptics being uncalled for and often giving rise to eczema. Under such treatment, in most instances, the swelling and irritation will subside and the ulcer become clean and more "healthy" in appearance, especially if the patient be confined to bed with elevation of the limb.

In cases where the skin will not tolerate moisture, or where the moist treatment seems unnecessary, the sore and its surroundings may be dusted with various powders, such as iodoform, dermatol, naphthalin, boric acid, europhen, orthoform, etc., either alone or in combination with starch-powder, as may be indicated. On account of its anesthetic properties orthoform would be an ideal remedy, especially in painful ulcers, if it did not occasionally cause excessive irritation and even gangrene. Hence it must be used with care, even when combined with other things. The Scott-Schley method consists in covering the ulcer thickly with pulverized boric acid, over which are placed several layers of rubber-tissue held in place upon the sound skin around the borders of the sore with adhesive-plaster. Over this is bandaged a protective pad of gauze. The dressing is not removed for from five to seven days or even longer. The results are said to be good.

(2) *Improvement of Blood-supply.*—Whenever possible *the patient should be kept in the recumbent position with the leg slightly elevated,* not only until the ulcer is closed, but until the scar has become sufficiently resisting to insure its further integrity. This always seems to the patient a useless waste of time, but in reality time is thus saved. It is by far the most important point in the treatment of ulcers of the leg in which poor circulation is a factor, but the plan must be carried out consistently in order to get the best results. It does not admit of occasionally walking about the house or sitting in a chair.

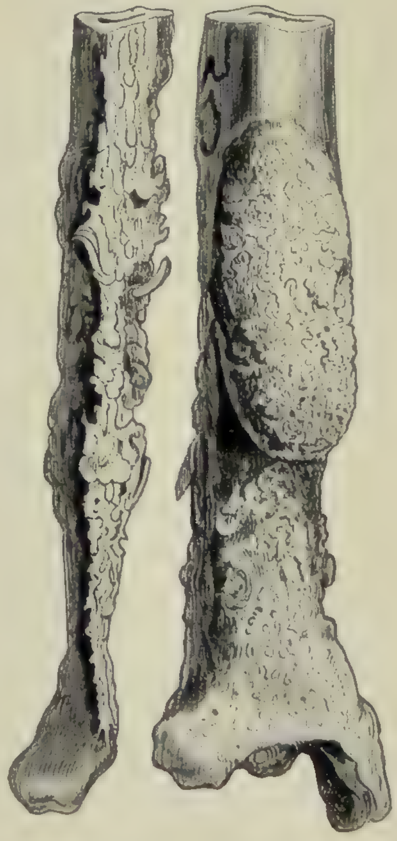

FIG. 69.—HYPEROSTOSIS OF THE TIBIA AND OSTEOPHYTES OF THE FIBULA DEVELOPING AFTER AN ULCER OF THE LEG (Musée Dupuytren) (Duplay and Reclus).

When circumstances do not permit of the recumbent treatment, the veins can be supported in various more or less effective ways. Bandages may be employed, made of plain rubber (Martin), rubber cloth, or woven bandages rendered elastic by the character of the mesh. Elastic stockings are excellent, but expensive and short-lived. Underneath the bandages the skin must be kept clean and well powdered, and it is best to prepare the leg, cleanse the ulcer, and apply the supporting bandages in the morning before any walking is done.

Unna's paste affords another method of obtaining support, which has been more extensively used abroad than in this country. It consists of gelatin 5 parts, zinc oxid 5 parts, boric acid 1 part, glycerin 8 parts, water 6 parts, and sometimes ichthyol 5 per cent. The limb is carefully cleansed, and the paste, which has been liquefied by warming in a water-bath, is brushed on from knee to foot. A gauze bandage is then applied, cutting it frequently instead of reversing in order to avoid wrinkles; then another layer of paste and another bandage until a sufficiently firm support of several thicknesses is obtained. If the ulcer has been covered in and is secreting freely, the dressing must be changed in a few days or a trap-door provided.

The method of *compression* suggested by Guérin is sometimes employed when the ulcer is small. It consists in enveloping the leg in cotton, over which a compression-bandage is firmly turned.

Strips of adhesive plaster, an inch in width, applied "shingle-wise" directly over the sore and reaching some distance above and below it (Baynton), may do good in old, callous ulcers without too much surrounding ezcema. The strapping should not encompass the entire limb for fear of embarrassing the circulation, and should be changed every few days, according to the amount of secretion. The indurated borders and base of the ulcer soon soften under the pressure and maceration, and strong granulations replace the weak ones. Sometimes a coin or piece of metal is placed under the plaster, although this is of doubtful utility. Philip recommends the strapping of ulcers with strips of more or less porous material, having adhesive substance upon their ends only, thus permitting the absorption of the discharges.

A useful procedure in many ulcers where the blood-supply is interfered with by surrounding cicatricial tissue, is to so loosen up the callus by *incisions* as to increase the circulation and permit of contraction of the granulating surface. *The method of Nussbaum* is probably the most effective. In this the ulcer is encircled at a distance of from one to two or three cm. by a cut completely surrounding it and reaching entirely through the thickened skin. Or a number of radiating incisions of a like depth may be carried from the center of the sore well out through the callous margin. Some recommend passing a tenotome beneath the ulcer and loosening its indurated base from the structures beneath.

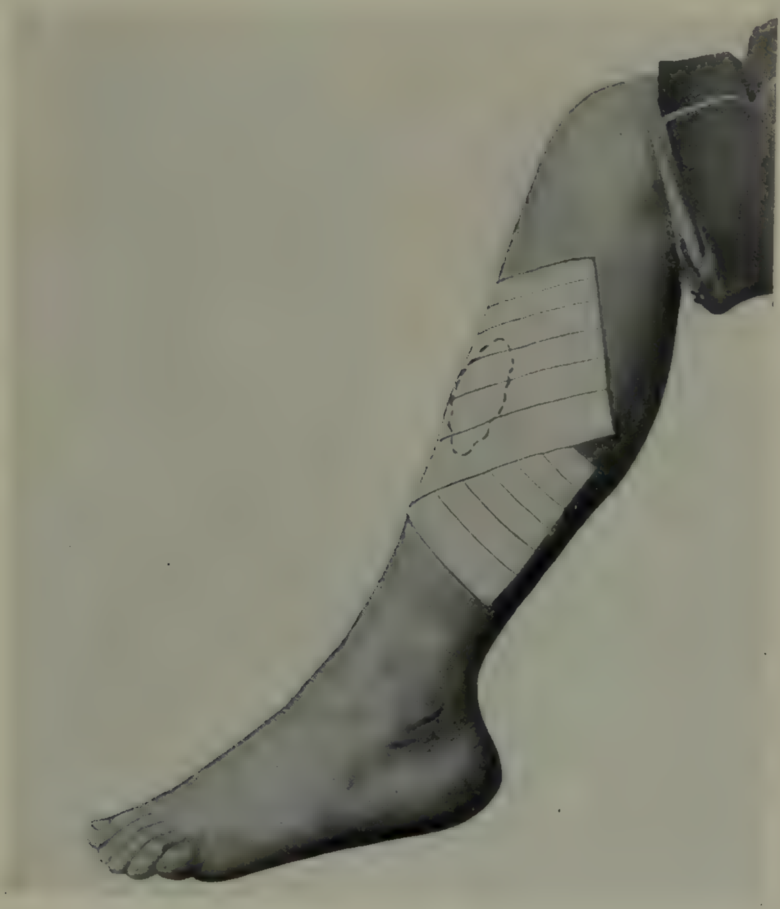

FIG. 70.—METHOD OF STRAPPING AN ULCER.

Thoroughly *scraping* an indolent ulcer or rubbing off the granulations with gauze will sometimes stimulate it to renewed activity, as will also *cauterization* every few days with stick silver nitrate, pure carbolic acid, 10 per cent. chlorid of zinc, 1 per cent. or 2 per cent. solution of ferri et potass. tart., etc., or the application of a *fly blister*. In certain *phagedenic conditions* even the actual cautery is recommended. Exposure of ulcers to the direct rays of the sun or the use of the X-ray or other forms of radiant energy have recently been highly spoken of, but it is yet too soon to come to a decision as to their value.

Operations upon varicose veins are frequently called for in aggravated cases, provided the general condition of the patient permit. These may consist in multiple ligations; in ligation of the internal saphenous alone; in extirpation of large or small sections of the varices; or in circumcision of the skin of the leg above the ulcer, or of the ulcer itself, tying all the veins and reuniting the cuticle. It must not be forgotten, however, that in the presence of an ulcer, infection of an operation-wound is likely to occur. (See Chapter on Surgery of the Vascular System.)

Stretching of the nerves supplying the area of skin in which the ulcer exists has recently been suggested (Bardescu and Chipault), and some good results have been thus obtained, even when allowance is made for the fact that the rest and attention incident to any operation will produce benefit in themselves.

Skin-grafting can often be resorted to with excellent results, provided the surface is protected from injury for several weeks following the operation by means of bandages, salves, and appropriate dressings. The best procedure is that of Thiersch, in which the surface is completely covered with thin shavings of epidermis from the thigh, it being better previously to curette away the granulations than to place the grafts on their untouched surface.

The Reverdin method, in which small clippings of epidermis are strewn over the granulations, and the method of Krause, in which large grafts from the entire thickness of the skin without a pedicle are employed, are less often used than the procedure of Thiersch and less reliable in their results.

Sometimes it may be desirable to employ a pedunculated flap from the vicinity of the ulcer or even from the opposite leg, when that is not also diseased. The raw surface left by such a plastic operation can in its turn be grafted according to Thiersch. (For methods of skin-grafting, etc., see Chapter on *Plastic Surgery*.)

In very bad ulcers, especially where the limb is completely surrounded, the ankle stiffened, the skin in a condition of elephantiasis, the muscles atrophied and the limb functionally useless, amputation is occasionally better than to consume time with ineffectual treatment.

Rodent Ulcer (*Jacob's Ulcer, Herpes exedens, Lupus exedens, Noli me tangere, Cancroid or Epitheliomatous Ulcer*).—This is a term much less frequently used than formerly to designate a variety of extremely chronic epithelioma of the face occurring in the cancerous age. It has a tendency steadily to increase in size, without glandular involvement, progressively consuming all the structures in its path, even cartilage and bone, until the features are more or less destroyed and hideous deformity results. It begins in the hair-follicles or glandular structures of the skin as a small crusted nodule. When the ulcer appears, it is deep, sharply outlined, almost painless, often with but little secretion, and with indurated edges and base.

The best **treatment** consists in the use of the X-ray or excision, rather than cauterization, which often hastens the destructive growth. After the use of the knife, extensive defects may be remedied by skin-grafting or plastic surgery. (See Surgery of the Skin.)

Mal-perforant, or **Perforating Ulcer of the Foot,** occurs in connection with a lowered resisting power of the tissues of the foot, due usually to some lesion of the nerves or vessels. The hand is rarely attacked. It is a circular, chronic, painless sore with callous borders, which eats progressively into the deeper soft tissues and bones and has little or no tendency to heal.

Etiology.—Although formerly looked upon as a specific disease, *mal-perforant* is now known to depend upon many local and general conditions of which it is an occasional more or less accidental manifestation. The various theories as to its immediate causation may be divided, according to Adrian, into—(1) mechanical, (2) vascular, (3) nervous, and (4) "mixed."

The *mechanical theory* regards injury as the sole cause, arising in most instances from the pressure or rubbing of a shoe. If this explanation were adequate, however, such ulcers would be very common, while in reality they are rare. Hence, although injury is undoubtedly of importance, some other factor must also be present.

The *vascular theory* assumes that arteriosclerosis is always present and causes ischemic necrosis through arterial and capillary thrombosis. Although it is true that vascular changes have been found in but comparatively few cases, nevertheless it is claimed that adequate search has seldom been made, and that even careful investigation may fail in the so-called nodular form owing to the nodules existing only at intervals in arteries showing few if any other alterations. (See Senile Gangrene.)

The *nerve-theory,* which is the one most commonly accepted, claims that perforating ulcer is always of trophic origin and depends upon chronic peripheral neuritis. In support of this assertion attention is called to certain interstitial and parenchymatous alterations frequently demonstrable in the nerves of the affected part. It must not be overlooked, however, that these nerve-changes may be due to secondary disturbances in nutrition depending upon arteriosclerosis, as in senile, diabetic, and other forms of gangrene.

The "*mixed theory*" assumes that either vessels or nerves or both may be at fault. It admits that traumatism is an important factor, although seldom if ever an exclusive cause.

In the light of our knowledge concerning vascular alterations and their relations to various gangrenous and necrotic processes (see "Gangrene"), I am inclined to agree with Fränkel, Lévai and others that mal-perforant, in the majority of instances at least, depends directly upon changes in the blood-vessels, which can most frequently be traced to disorder of the nerves, but which may be due to other causes, such as diabetes, chronic alcoholism, syphilis, etc. According to this view, the degenerative nerve-lesions found near the ulcer are secondary and unessential phenomena due to faulty nutrition.

Perforating ulcer is observed in connection with various diseases and conditions, the most prominent of which are: locomotor ataxia, fractures of the spine with injury of the cord, leprosy, diabetes, chronic alcoholism, syringomyelia, spina bifida, progressive paralysis, progressive muscular atrophy, arteriosclerosis, syphilis, peripheral neuritis, injury and division of peripheral nerves, etc.

Perforating ulcer from lesions of the central nervous system is comparatively rare, and it is doubtful if it is ever due to embolism or to ligation of an artery. Burns and scalds and particularly frost-bites are sometimes responsible.

The three most prominent causes are affections of the spinal cord, injuries of the peripheral nerves, and diabetes mellitus. In diabetes the vitiation of the tissues from the presence of sugar is considered by Adrian to be the sole cause of the ulcer; but it seems reasonable to suppose that vascular sclerosis also plays a prominent part, as it does in diabetic gangrene.

Heredity is of no importance except in so far as it bears upon the occurrence of such diseases as may give rise to mal-perforant. The malady is seen more frequently by far in males than in females, and is almost exclusively confined to adults, especially between the ages of forty and sixty. Its rare appearance in children is nearly always associated with spina bifida. Occupations requiring much standing and walking are strongly predisposing, provided a tendency to the disease already exist. Ill-fitting shoes and deformities of the feet giving rise to excessive pressure or irritation are of much importance in determining the appearance and location of perforating ulcers.

It has been asserted that suppurative bursitis is a frequent cause, but in view of facts already stated this view is untenable; although it must be admitted that ulcers arising from bursitis are often quite similar to mal-perforant in superficial appearance.

Symptoms.—Perforating ulcer has a marked tendency to develop where pressure and irritation are greatest, which is almost always upon the sole of the foot at the juncture of the great or little toe with the metatarsus. It may occur, however, upon the heel, the sides of the foot, the plantar surface of any portion of the great toe, or even upon the center of the sole, these unusual situations being most common in diabetes. When talipes or hammer-toe exists, the sore is apt to occur wherever pressure is pronounced, even upon the dorsum of the foot or ends of the toes. Usually but one foot is affected, although both feet may be involved, in which case the disease is often symmetrical.

Three stages may be recognized in the development of the ulcer: (1) the formation of callosities, (2) superficial ulceration, and (3) deep ulceration. Occasionally, especially in tabes and in diabetes, a purulent blister is the first indication of trouble; but usually a marked epithelial thickening, in the form of a corn or bunion, is the initial symptom. Sooner or later the center of the callosity breaks down into a bluish, unhealthy, indolent, superficial ulcer, secreting a watery pus, small in amount and offensive in odor. The ulcer is circular as though punched out of the callous tissue, the latter being at times so thick and overhanging that the sore is almost concealed beneath it. There is little or no tendency to heal, even under the best of treatment, and if recovery should take place a speedy relapse is the rule, even though the patient remain quietly in bed.

The indolent and often foul ulcer tends to eat deeply into the subjacent tissues, progressively involving bursæ, tendons, muscles, joints, and bones. A deep, round hole results, which may even perforate the foot. The most striking symptoms are chronicity, stubborn resistance to treatment, and absence of tenderness and pain, although in diabetes more or less sensation may be present.

The fact that perforating ulcer is so often found with lesions of the nervous system accounts for the abnormalities of sensation, motion, and the reflexes, which frequently accompany it. This also explains the various trophic disturbances which are often observed, such as excessive epithelial growth, not only in the vicinity of the ulcer, but occasionally over the entire foot and leg; also eczema, erythema, pigmentation, abnormal growth of hair, and excessive perspiration. The nails are frequently thickened and distorted, and the subcutaneous cellular tissue so changed as to even suggest elephantiasis.

Inflammatory complications, sometimes serious, are not uncommon, owing to infections through the ulcer; and an ascending neuritis may even result in myelitis. Gangrene from arteriosclerosis may appear.

Treatment.—In those predisposed to mal-perforant (diabetics, sufferers from tabes, etc.) prophylaxis deserves consideration. The shoes must fit accurately and without undue pressure, much walking is to be avoided, and callosities should be carefully pared and relieved from pressure.

When ulceration has begun, the recumbent position and cleanliness are of paramount importance, as in other ulcers of the lower extremity. The callous epidermis should be removed so as to render the sore as superficial as possible, dead bone must be scraped away, or extracted if in form of a sequestrum, and drainage must be perfected by enlarging the opening, slitting up stagnant pockets, etc. It must be emphasized, however, that operative intervention should be undertaken with care and discrimination, owing to the tendency of the devitalized tissues to necrosis and infection.

Periodic curettements and cauterizations with silver nitrate or pure carbolic acid are often of service, as is also the employment of dry iodoform gauze used as a packing, together with the occasional use of moist bichlorid dressings.

Both the constant and interrupted currents have been used with benefit, sometimes locally and sometimes applied to the spinal cord or afferent nerves. Measures directed toward improvement of the circulation of the foot, such as massage and stimulating baths and lotions, are occasionally of some importance.

The initial cause of the trouble must receive attention, because upon its successful handling depends a cure much more than upon local measures. Diabetes, syphilis, and diseases of the nervous system should receive appropriate and energetic treatment.

In bad cases, especially where gangrene or serious infections exist, amputation may be required; but unless this can be done in sound tissues with adequate innervation, a perforating ulcer may develop upon the stump where it is exposed to the pressure of an artificial limb. Resections of joints are usually of little benefit.

The most satisfactory operative results have been obtained by stretching the posterior tibial nerve, together with scraping the ulcer, or better excising it and uniting the wound by immediate suture (Chipault). The operation is best done through a curved incision beneath the internal malleolus, the nerve being isolated and vigorously stretched in both directions by means of some blunt instrument inserted beneath it. Sometimes the external or internal plantar nerve alone is treated in this manner. In addition to stretching, Delagenière separates the individual nerve-fibers from each other with the point of a needle. Out of 79 cases, Chipault reports 69 recoveries and claims that the results are permanent.

Curling's Ulcer is an ulcer of the upper portion of the duodenum following a burn of the skin in any portion of the body. It is a rare complication and develops during the stage of inflammation and sloughing. It is probably embolic in origin, as would be suggested by its round and punched-out appearance. Like other ulcers of this portion of the bowel, it is apt to cause pain or discomfort from one to three hours after eating, when the pylorus opens and the contents of the stomach pass out. It may give rise to hemorrhage from the bowels or stomach, but not necessarily so. A tender spot is usually present in the epigastrium.

The **treatment** can be conducted on the general line of more or less absolute rest of the stomach, obtained, if the patient is not already too much weakened, by rectal feeding; but the surer method of handling such cases, when refractory, is by gastro-enterostomy. Operation is of course required without question in cases of perforation or persistent hemorrhage.

Trophic or Neuroparalytic Ulcers arise from disturbances of the nerves or nervous centers. Absence of sensation in the part affected, together with vasomotor disturbances, are probably of more importance in the causation than lesions of the "trophic nerves," which are somewhat problematic to say the least. These ulcers follow fracture of the spine with paralysis, division of nerve-trunks, such as the sciatic, and also various nervous troubles and continued fevers, for instance, typhoid. They appear and grow sometimes with amazing rapidity, a few days sufficing to produce a large loss of substance. In all such cases the back should be examined daily and preventive measures instituted from the start.

Absolute cleanliness, relief of pressure, and sometimes light cauterization with silver nitrate or carbolic acid are indicated, together with the application of an antiseptic powder or a salve, as may seem best under the circumstances. Pure bovinine often gives excellent results. Such sores are difficult to heal and have a strong tendency to relapse. (See "Bedsores" in chapter on Gangrene.)

A **Scirrhous ulcer** is one occurring in connection with a scirrhous carcinoma, usually of the breast. It is in most instances sharply excavated within a bed of solid carcinomatous tissue. Although skin-grafting is sometimes resorted to for temporary relief from hemorrhage and offensive discharges, which are often present, the only cure is complete extirpation of the cancer, or in rare instances the use of the X-ray.

A **gouty ulcer** is one occurring in connection with gout, particularly at the site of an uric-acid deposit; for instance, over the metatarso-phalangeal articulation of the great toe.

The term **putrid ulcer** is sometimes used to designate certain forms of phagedena or hospital gangrene.

Round or peptic ulcer is found in the stomach, duodenum, or in the upper portion of the jejunum, where it usually follows a gastro-enterostomy. The pyloric end of the stomach is its favorite site. It is accompanied by hyperchlorhydria, is apt to be multiple, and has a tendency to perforate into the peritoneal cavity. Hematemesis occurs in a considerable proportion of the cases, and perhaps melena, while pain or discomfort following the taking of food at a greater or lesser interval and gaseous distention are almost universal.

The **treatment** is based on rest and regulation of diet, or improvement of gastric drainage by pyloroplasty or gastro-enterostomy. (See chapter on the Esophagus and Stomach.)

Senile Ulcer is an indolent sore, usually callous and pigmented, occurring on the limbs of old people and due to various causes. It is often associated with enlarged veins.

A **Phagedenic Ulcer** is one in which the infection is so intense, or the resisting powers of the tissues so low, that rapid spreading with sloughing takes place without the formation of protecting granulations. Such an ulcer has sharp, gnawed-out, undermined and swollen edges, and the surrounding skin is apt to be more or less dusky from impaired circulation. Its surface is covered with sloughing tissue and foul, ichorous discharges, instead of clean granulations and ordinary pus.

When the progress is very rapid and the sloughs unusually large, the process is known as *sloughing phagedena.*

Phagedenic ulcer was formerly frequently met with under the septic conditions then so universally present in hospitals and elsewhere, and especially was this true in barrack- and tenement-life; but at the present time it is fortunately rare, being met with occasionally only, principally in connection with venereal sores and old neglected ulcers of the leg. Although the disease is directly caused by a mixture of various micro-örganisms, its peculiarities are due more to lack of general or local resisting power than to the exact nature of the infection, a debilitated constitution being an important factor, such as may accompany syphilis, alcoholism, the morphin habit, poor hygiene, scurvy, etc.

Venereal phagedena most often begins beneath a tight prepuce, where the poisonous secretions are confined under tension and the distended tissues are deprived of proper circulation. It may rapidly destroy not only the entire prepuce, but a portion or all of the glans as well. The female genitalia may be largely eaten away and perhaps the rectum or bladder invaded.

In the groin the process originates in an ulcerated bubo and may be so extensive in its inroads upon the surrounding parts as to endanger the femoral vessels. When the leg is affected, the skin may be rapidly destroyed around its entire circumference, and the muscles and even the bones and joints invaded.

Treatment must be vigorous and applied with the idea of removing sloughs and destroying infection. Where the case is urgent a general or local anesthetic should be employed, and all the dead tissues, including the borders of the ulcer, removed with curette, knife, and scissors. This should be followed by a thorough cauterization with the actual cautery, pure carbolic acid, bromin or fuming nitric acid; after which a moist antiseptic dressing or a dry dressing of iodoform, aristol, or some other powder is applied.

Many mild cases, however, may be successfully treated by antiseptic applications, preceded by the use of pure carbolic acid, which is particularly suitable for such a purpose on account of its anesthetic properties. As a general rule, warm moist antiseptic compresses (bichlorid 1 to 5,000, 10,000 or 15,000) are preferable to powders, especially if the case is at all severe. (See chapter on Gangrene.)

ULCERS IN DIFFERENT REGIONS.*

Anus.—Syphilitic, chancroidal, tuberculous, and malignant sores are not uncommon in this vicinity, both within the bowel and upon the surface of the skin. The usual form is the so-called *fissure-in-ano*, which is a small ulcer, more or less elliptic in form when the anus is dilated, but assuming the appearance of a crack or fissure, such as occurs on a chapped lip, when the orifice is contracted. The ulcer lies parallel with the axis of the bowel and within the grasp of the sphincter, some of the fibers of which are often seen exposed in the floor of the ulcer. A small, so-called "sentinel pile" marks its extremity. Such ulcers have almost no tendency to heal, on account of muscular activity and the passage of fecal matter. They give rise to pain, often intense, and a burning sensation during and for some time after stool, accompanied often by discharges of blood. The **treatment** consists in dilating the sphincter muscle under general or perhaps local anesthesia.

Ingrowing nails are found upon the fingers under exceptional circumstances, but their almost invariable location is upon the toes, especially the great toe. They are caused by too short or too tight shoes, the pressure from which gradually pushes the skin up over the edges of the nail on one or both sides. This is often aided by overlapping of the second toe and by the patient's trimming away the corners of the nail until they dig into the elevated skin instead of projecting beyond it.

If the affection is at all severe ulceration soon sets in, accompanied by pain and inflammation, thus inhibiting the function of the foot.

In treating these cases it is usually better to proceed at once to operation rather than consume time with cauterization of the ulcer and the painful insertion of lint, tinfoil, etc., beneath the edge of the nail, as is often recommended. Under local anesthesia (cocain, ethyl chlorid), or the use of ethyl chlorid, nitrous oxid, or somnoform as a general anesthetic, the side of the toe, including the entire fold of overlapping skin, is shaved off with a scalpel, and a portion of the deformed nail extracted. In very severe cases a part or all of the matrix is likewise removed. Flap operations are sometimes done, or skin-grafting resorted to, in order to cover in the raw surface and lessen the time of healing.

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* Consult also the chapters dealing with these various regions.

Ulcers of the Leg (Crural Ulcers).—The leg is a favorite location for ulcers in those who have reached middle life and beyond, the varicose ulcer described above being by far the most common. Other forms are the simple ulcer, the syphilitic, the tuberculous or scrofulous, the typhoid, the malignant (Marjolin's, Jacob's), and a number of other more or less distinct varieties occurring principally in the tropics—Aden or Yemen ulcer, Cochin China ulcer, Delhi ulcer, etc.

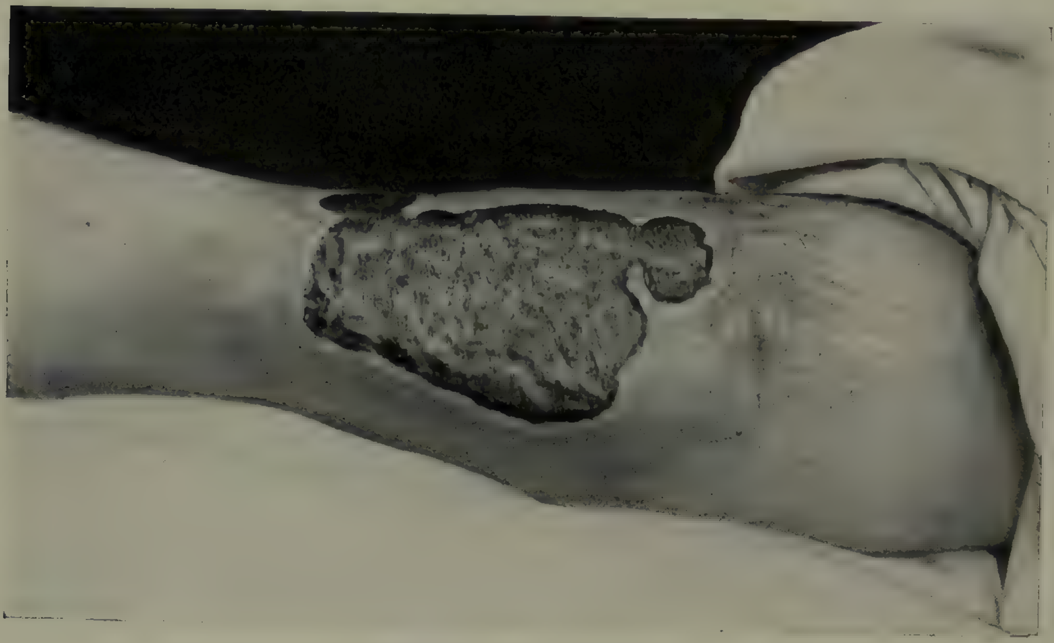

Fig. 71.—Ulcer of Leg.

Simple ulcers should be treated antiseptically, according to general principles; the syphilitic variety requires specific medication (potassium iodid internally and mercurial plaster locally); the malignant form must be thoroughly extirpated or an amputation done; while tuberculous sores must be curetted or excised according to circumstances. An important factor in the treatment of crural ulcers is a recumbent position with elevation of the limb, particularly when defective circulation is present, as in varicose veins; although the wearing of an elastic bandage or stocking may answer the same purpose to a limited extent.

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CHAPTER VIII.

MORTIFICATION OR GANGRENE.

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DENVER, COLORADO.

DEFINITION.

Theoretically the term gangrene applies to the death of considerable portions of any kind of tissue as a whole and while still attached to the body. Practically, however, there is an increasing tendency to limit its use to death of the soft parts alone, or to these and the bones which they may contain, as in gangrene of an extremity, especially when the lifeless portion has an inclination to become dark in color and undergo decomposition or mummification. In the case of internal organs and tissues, unless putrefaction and decomposition are manifest, the word *necrosis* is almost invariably employed instead of gangrene, as it also is in connection with bone.

The death of tissue in mass is likewise designated as mortification, mummification, anthraconecrosis, sphacelation, and sloughing, according to its character.

Mortification is a term synonymous with gangrene and in common use among those outside the medical profession.

Mummification, or *anthraconecrosis,* is a form of gangrene in which the tissues become dried or mummified. It is often observed in old people.

When the whole or a large portion of an extremity dies, the dead part is sometimes spoken of as a *sphacelus* and the process as *sphacelation.* The term is also loosely employed in connection with ulceration and sloughing.

During the course of ulceration or severe inflammation, as in abscess or cellulitis, areas of tissue may succumb, the "core" of a boil being an excellent illustration. These dead masses are known as *sloughs* and the manner of their formation as *sloughing.* If the sloughs are large and become dark and perhaps putrid, they are designated as *gangrenous sloughs,* and the process as *sloughing gangrene.*

Ulceration occurs in connection with an open suppurating surface, the tissues melting imperceptibly into the purulent excretions. It is often combined with sloughing and gangrene.

Necrosis is a generic term covering all varieties of tissue-death; but it is also specifically applied to those forms which occur in internal organs without decomposition, and to the death of bone in mass, the necrosed bone being called a *sequestrum.* Tuberculous and other microbic lesions, for instance, are usually accompanied by necrosis, and necrotic areas result from infarction and other circulatory and nutritive disturbances.

Necrobiosis refers to a slow loss of vitality preceded by various degenerative changes, such as occur in poorly nourished or slowly poisoned tissues.

These various forms of local as opposed to general death are all so closely related to each other that no distinct line can be drawn between them.

CAUSES.

These may be divided into two main groups: (1) those producing direct and immediate death of the tissues, and (2) those leading indirectly to gangrene by arrest of the circulation of the blood. In the latter thrombosis plays a leading part and is almost always present, according to the newer pathology.

1. The **direct causes,** producing immediate cellular death, are:

(*a*) *Chemical,* including *bacterial toxins* and *animal poisons.* The action of ordinary chemicals is usually superficial, so that they rarely produce gangrene of more than the skin or mucous membrane with which they come in contact. The poisons of bacteria, on the other hand, often act deeply and widely throughout the soft parts, as in spreading gangrene. Although microörganisms are found in abundance in most gangrenous tissue, this does not mean that they are always the cause of the trouble. In fact, they are often merely secondary contaminations.

(*b*) *Mechanical,* in which the protoplasm of the cells is killed by direct physical injury. It can readily be understood that gangrene from this source must be comparatively rare, except in small areas. It requires extraordinary violence with complete crushing of the tissues, such as occurs when the wheels of a railroad-car pass over an extremity.

(*c*) *Heat and Cold.*—These, particularly the latter, frequently act through the circulation, by means of thrombosis, as well as directly upon the tissues.

2. The **indirect causes,** acting through stoppage of the circulation, are:

(*a*) *Injury of blood-vessels,* locally or at a distance. This includes injury from mechanical sources, such as crushes and gunshot wounds, from bacterial toxins, animal and other poisons, heat, cold, and ordinary chemicals of various kinds. An injury may completely or partially divide a vessel; or simply bruise it and lacerate its internal coat, causing a thrombus; or "weld" together its opposing walls, as may occur from a severe blow against a bone (Unna).

(*b*) *Diseases of blood-vessels,* particularly arteritis, arteriosclerosis, and atheroma, leading ordinarily to obstructive thrombosis and rarely to complete obliteration by thickening of the inner coats. Under this heading may also be classed alterations of the intima from lack of nutrition, or from desiccation of the surrounding tissues. Most, if not all, cases of "spontaneous gangrene" may be referred to this source.

(*c*) *Embolism.*—Emboli may be formed of clots, fibrin, pus, etc., or of living bacteria alone.

(*d*) *Vascular disturbances due to nervous influences,* consisting in spasm or paralysis of arterioles. "Trophic gangrene" is more probably caused in this way than through special trophic nerves governing nutrition, thrombosis preceded by nutritive alterations in the vascular intima being the most prominent factor. The gangrene produced by cold or by the long-continued action of certain drugs, such as ergot, as well as Raynaud's gangrene, gangrenous urticaria, etc., are explained by many in a similar manner, but it is always a question as to whether the mortification is due directly to vascular spasm, or arises secondarily from alterations in the intima followed by obstructive thrombosis, with the chances in favor of the latter.

(*e*) *Mechanical closure of vessels,*—by ligation; by constriction of a part, for instance, with a tight bandage; by long-continued pressure, as from a tumor or from the bed during a protracted illness; or by overstretching of the tissues, as may occur in plastic operations, or in the closure of wounds.

It will be appreciated from a consideration of the above classification that gangrene is, in the vast majority of instances, due to arrest of the circulation of the blood, which is brought about principally by thrombosis. Obstruction of the main artery or vein, however, does not cause gangrene when there are collateral vessels, unless these are also obliterated.

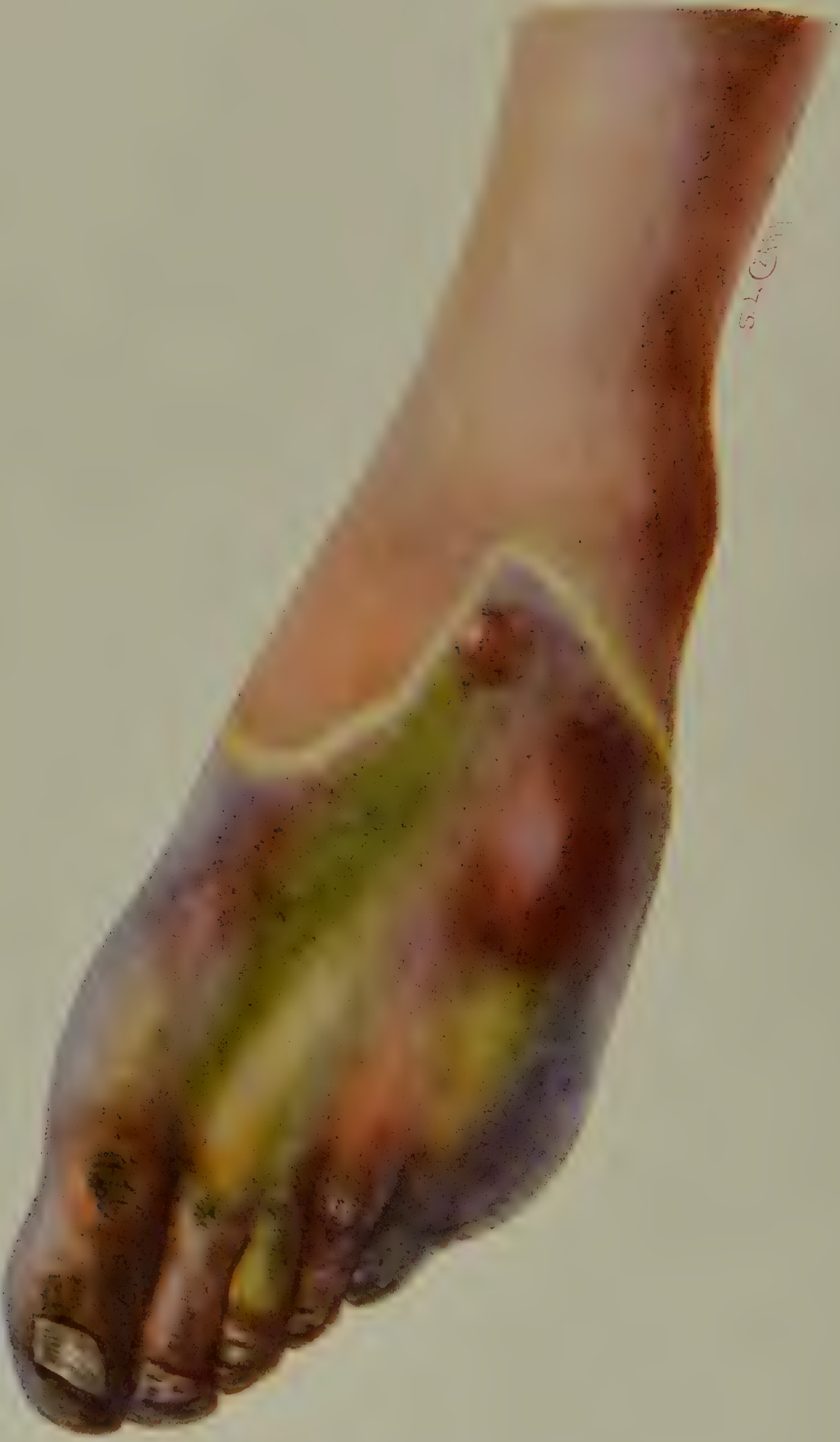
Any of the numerous causes of gangrene may be greatly aided by general conditions which weaken the resistance of the tissues, such as diabetes, nephritis, syphilis, scurvy, various fevers (especially typhoid), a weak heart, age, bad hygiene, drug-habits, alcoholism, and debility from overwork and lack of proper rest; while the dangers and extent of the process are often increased by the growth of bacteria, which generally gain entrance through an external wound.

GENERAL CONSIDERATIONS.

When gangrene occurs and the sphacelus remains full of blood and exudates, the condition is known as **moist** or **acute gangrene.** This is usually due to sudden stoppage of the arterial circulation. The blood remains in the tissues because there is not sufficient force behind it to push it out; and extensive exudation takes place because of loss of vitality and tone in the walls of the vessels. In addition to this, when the main artery is suddenly torn or plugged, the circulation is not often completely cut off at once, a little blood being able to enter through collateral vessels, thus adding to the stagnant fluids already in the lifeless part. Gangrene following direct injury, such as a crush, or succeeding an injury to a main vessel at a distance, as occurs in gunshot wounds, is almost always moist.

Rarely complete cessation of the venous circulation is at fault. But simultaneous interference with arterial supply and venous drainage is fairly common, being most often met with in injuries, especially those cacompanied by the formation of a large hematoma, the pressure of which interferes with vascular function. This is strikingly illustrated in wounds of the popliteal artery with bleeding beneath the deep fascia

PLATE VII.



Moist Gangrene of Foot (Jefferson Medical College Hospital, Phila.).

followed by gangrene of the leg. (See chapter on Surgery of the Vascular System.)

Inflammation can also cause moist gangrene; sometimes by direct pressure of the exudates on the afferent and efferent vessels, but generally by thrombosis. When it seems to arise from the action of microörganisms alone (*microbic gangrene*) a rapid thrombosis of smaller arteries and veins is probably at fault, as well as the direct action of bacterial toxins upon the cellular protoplasm.

The immediate aspect of an extremity affected with mortification of the moist variety depends largely upon the amount of blood present when death occurred, which may have been augmented by influx from the collaterals even though the main artery is plugged. In inflammatory lesions, for instance, swelling of the part and dusky redness of the skin are always present; and in crushing injuries a reddish, bluish, or blackish tinge is often imparted to the surface by the contained blood. But when the trouble is due to sudden arrest of the arterial circulation, especially if the collateral supply is cut off by thrombosis or the pressure of a clot, the appearance is quite different. There is no swelling or discoloration. The skin is deathly-white and cold, and perhaps marbled with blue veins; and if it is pinched into a fold it will not flatten out again immediately, owing to loss of its normal elasticity. The pulse is, of course, absent and sensation gone. In fact, the limb looks as though it had already been amputated.

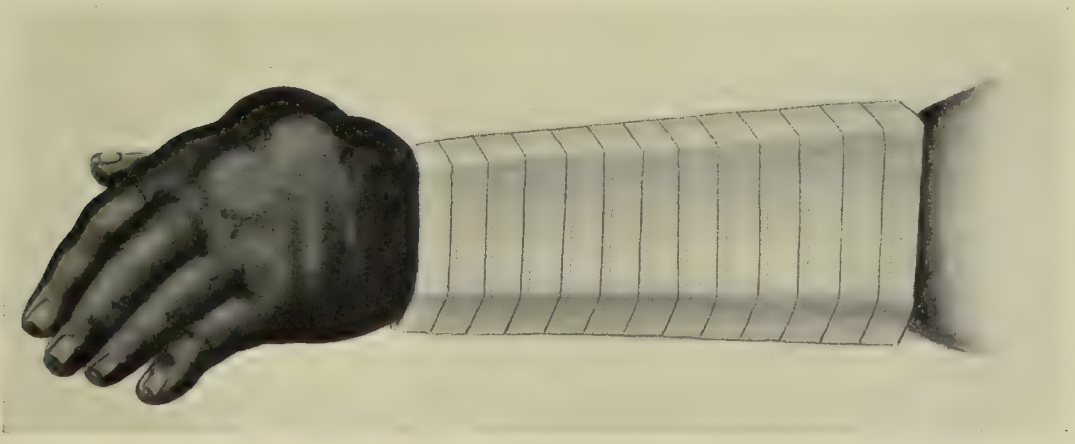


Fig. 72.—Gangrene Resulting from Tight Bandaging (Duplay and Reclus).

Regardless of original appearances the later changes of moist gangrene are constant and characteristic. From exudation of blood-pigment and putrefaction, the cutaneous covering becomes brownish, and finally brownish-black, or even black or green. A mottling of the surface is not uncommon. The epithelium frequently rises in large blisters containing serum exuded from the vessels, which is possibly foul and stained with blood-pigment. (See Plate VII.) In fact, the entire epithelial layer becomes loosened, and may easily be slid around upon the firmer portion of the skin beneath.

There is nearly always swelling—marked in the congestive, and slight in the anemic form. This is due to collateral circulation, to exudation, to infiltration of fluids from adjacent living tissues, and to the formation of gas from bacterial growth.

The muscles, which are dark in the *congestive form* of gangrene and of a dirty yellowish tinge in the *anemic form*, soon begin to soften and disintegrate structurally. Their elements lose the receptive power for anilin stains together with their structural outlines, until they finally approach a slimy fluidity; the whole limb, with the exception of bones, tendons, and the tougher fasciæ, being transformed into a more or less homogeneous, putrid mass.

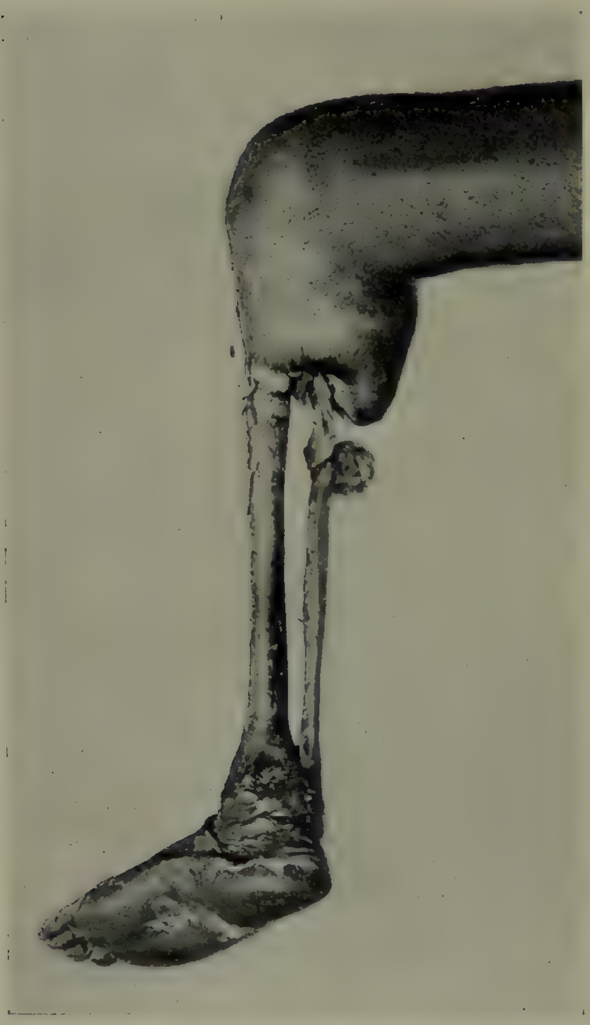


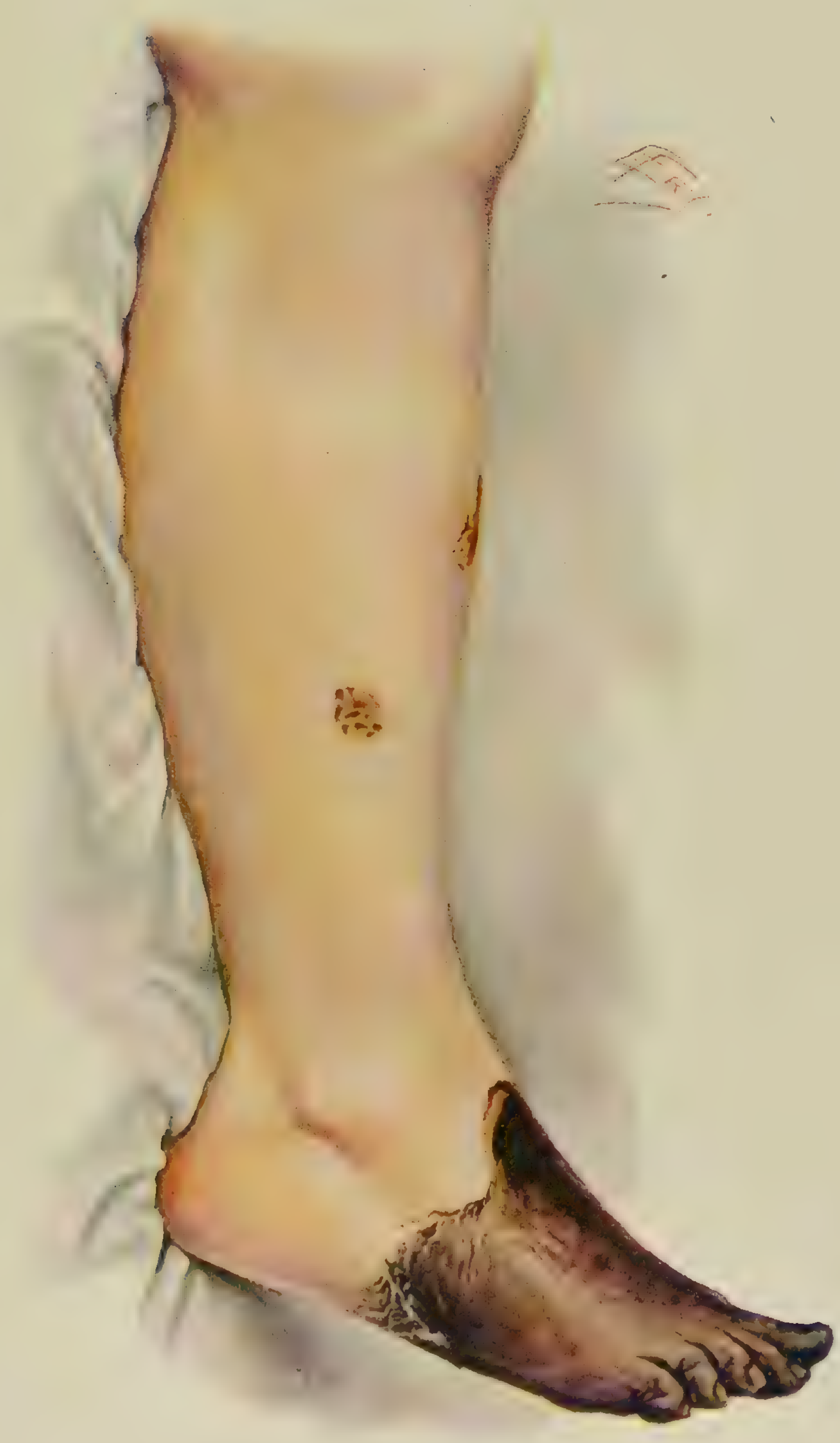
Fig. 73.—Spontaneous Amputation in Progress as a Result of Gangrene Probably due to Arterial Embolism during Malarial Fever. (Photograph furnished by E. Owen Thurston, Esq., Calcutta. "Lancet," 1905, i, 1331.)

The characteristic phenomena of moist gangrene, which if the patient live long enough is always accompanied by decomposition and putrefaction, are in large measure due to the growth of microörganisms. These are not specific in character, but they are often gas-forming and anaërobic. Even the so-called *gangrène foudroyante* is not due to any one bacterium, but may be caused by several different species. The germs of putrefaction are most often encountered, the formation of obnoxious gases being due to their growth; but any microörganism capable of developing in dead animal-tissue may also be present, including those of suppuration, although, of course, pus can never be formed except at the junction of the dead tissues with those which are still alive.

Microbic gangrene is always moist in character and is often characterized by the formation of gas, which renders the tissues emphysematous, so that they crackle like parchment when pressed upon, the gas exuding in bubbles when the skin is incised. The profuse growth of bacteria in a gangrenous limb may cause unlimited and rapid extension of the process without reference to previous circulatory disturbances or injury of the tissues (*infective spreading gangrene*).

Dry or chronic gangrene rarely develops suddenly. It is a slow process in which the tissues are gradually deprived of blood through de-

PLATE VIII.



Dry Gangrene (Coley).

fect in the arterial circulation—usually arteriosclerosis complicated by thrombosis. The blood and other fluids have ample time to drain out of the limb through veins and lymphatics while stoppage of the circulation and death of the part is occurring, thus leaving the tissues comparatively dry. Further desiccation may then take place through evaporation, until the part becomes shriveled and often so hard that it fairly rings under the tap of a finger-nail (*mummification*). The color is brown, blackish-brown, or even quite black, owing to extravasated blood-pigment and to color-changes in the tissues from deprivation of moisture and disintegration. (Plate VIII.)

Between moist and dry gangrene all gradations are found, both varieties often existing side by side; whether the process takes one form or the other frequently depending upon the presence or the absence of bacterial infection and decomposition.

Most forms of gangrene eventually limit themselves to a certain area, the line between the dead and the living being known as the *line of demarcation.* Here is massed an army of polynuclear leukocytes and proliferated tissue-cells whose duty it is to protect the body against injurious substances and help rid it of dead and useless tissues. An inflammatory process is thus set up which is soon followed by suppuration, and an ulcerating furrow develops between the gangrenous and the living parts, the first manifestation of which is a purulent blistering of the epithelium with redness and exudative thickening upon the proximal side. The bone, of course, resists much longer than the soft parts, and hence the peculiar condition may result of a dried or more or less putrid and disintegrating foot attached by a section of bare bone to the cicatrized stump of a leg above. When the bone gives way, *spontaneous amputation* will have resulted, the stump being conical from projecting bone (Fig. 74). Hemorrhage practically never occurs during this process because the vessels are effectively closed by thrombi in advance of their dissolution.

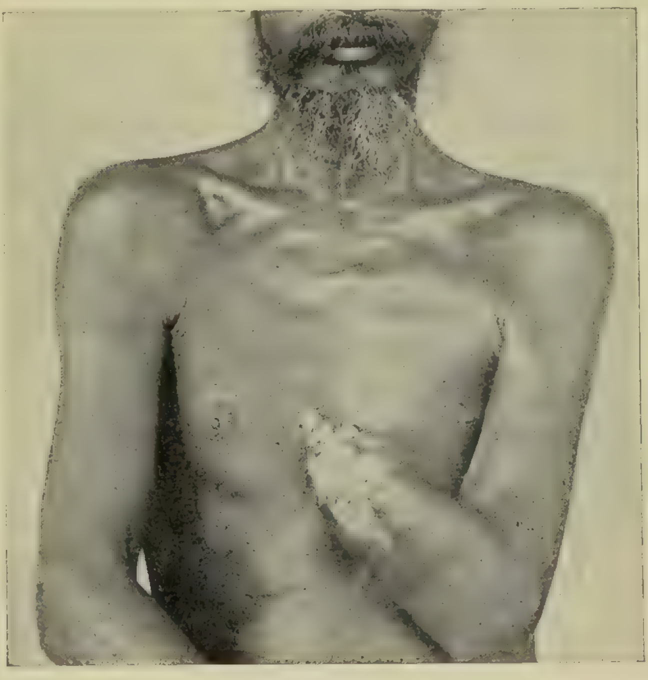


FIG. 74.—SPONTANEOUS AMPUTATION AS A RESULT OF GANGRENE FROM ARTERIAL THROMBOSIS.
(Photograph furnished by E. Owen Thurston, Esq., Calcutta. "Lancet," 1905, i, 1331.)

The origin of pain in gangrene is obscure. By some it is ascribed to inflammatory or degenerative changes in the nerves, and by others to acute anemia reacting upon nerve-tissues. Perhaps both of these factors play a part. In embolic gangrene the severe pain occurring exactly at the point of arterial obstruction suggests that the shock and irritation of the embolus itself is markedly concerned in the phenomenon.

CLINICAL FORMS OF GANGRENE.

Senile gangrene (sometimes called *chronic* or *Pott's gangrene*) is a typical form of dry gangrene of the lower extremities, rarely of the upper, occurring in old people. It depends upon narrowing of the lumen of the arteries by sclerosis or atheroma, which is followed by complete thrombosis.

It was formerly taught by von Winiwarter, and is still maintained by many, that senile gangrene is due to a definite form of inflammation of the internal coats of the arteries (endarteritis), which produces narrowing and finally obliteration of their channels by the formation of granulation-tissue; and that vascular sclerosis, thrombosis, and atheroma, which is merely a later stage of sclerosis, have nothing to do with the process and should be disregarded. But the pathologic researches of Zoege-Manteuffel and Weiss have recently demonstrated that the principal if not the sole cause is probably sclerosis. This narrows the arterial caliber to a point where thrombosis easily occurs on the roughened surface, thus completing the obstruction. What was formerly described as granulation-tissue spring-

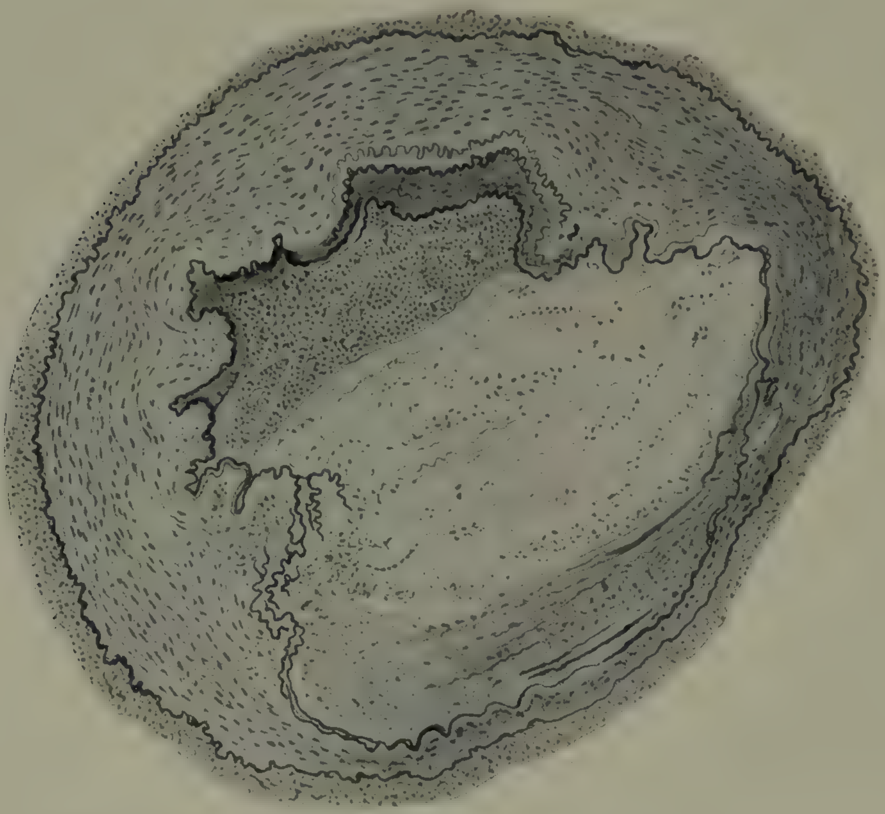


FIG. 75.—GREAT STENOSIS OF LUMEN OF DORSALIS PEDIS ARTERY BY A PLAQUE OF SCLEROSIS. OBSTRUCTION OF THE REMAINDER OF THE LUMEN BY AN ORGANIZED THROMBUS (Bunge).

ing from the intima is really more or less definitely organized thrombi, as is shown, among other things, by the remnants of blood-pigment which it frequently contains (Figs. 75, 76). A weakened heart and a debilitated bodily condition have little to do with senile gangrene, except as they favor the formation of thrombi and lessen the vitality of the tissues themselves.

Arteriosclerosis is of two kinds, which often coexist—the diffuse form and the nodular form. It is the latter which usually causes gangrene, by forming isolated or multiple nodules, sometimes in the nature of atheromatous plaques, which project into the arterial lumen and invite coagulation of the blood. These are sometimes difficult to detect post-mortem because the remainder of the artery may be almost if not quite normal, which accounts for the condition having been frequently overlooked. These sclerotic nodules tend to occur wherever arterial branches are given off; hence the thrombi which ensue are apt to obstruct the collateral as well as the main circulatory channels, thus hopelessly depriving the limb of nutrition.

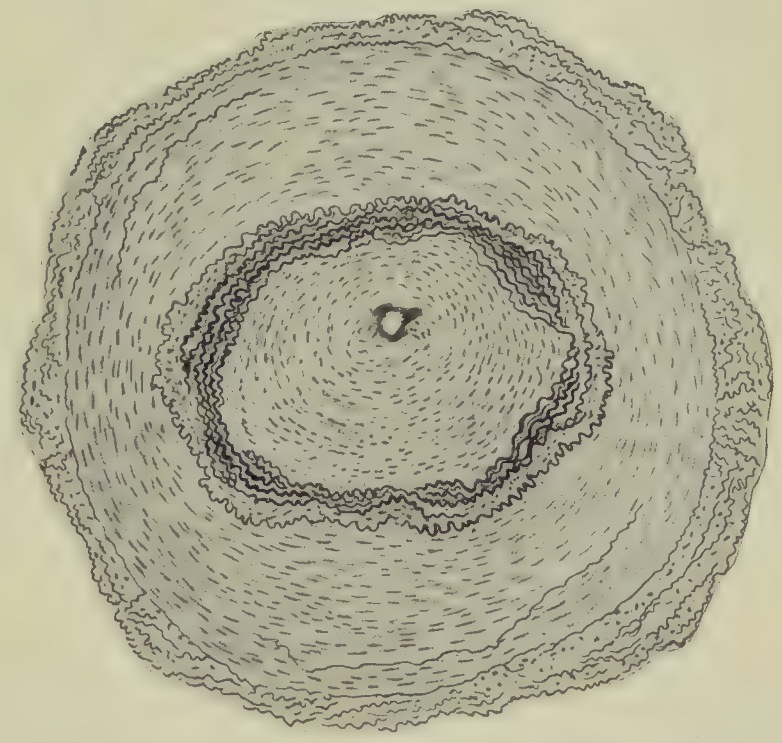


Fig. 76.—Obstruction of an Artery of the Toe. Concentric Sclerotic Increase in Thickness of the Wall (Bunge).

The degenerative changes often found in the nerves and perineural tissues do not indicate that senile gangrene is of nervous origin, as has been supposed; but they are rather an expression of poor nutrition dependent upon defective circulation.

"Senile gangrene" is not confined to old people, as its name would seem to indicate, but is often found in middle life and even in those who are much younger; depending upon the fact, which is receiving more and more general recognition, that arteriosclerosis is not exclusively a lesion of the aged. In the young the disease is called *spontaneous* or *pre-senile gangrene*, the latter being the preferable and more expressive term. In addition, it is now almost universally accepted that gangrene appearing during the course of diabetes mellitus is also due to arteriosclerosis and not merely to the presence of sugar, except in so far as sugar is responsible for the vascular lesions.

Symptoms.—An early diagnosis of impending senile gangrene may permit of its indefinite postponement by appropriate treatment, hence the *prodromal symptoms* are of much importance. These consist in disturbances of circulation, sensation, and function. The foot of the affected extremity is cold and numb, or it is the seat of tingling sensations and perhaps of shooting pains. Its color is cyanotic or mottled, and the whiteness resulting from the pressure of a finger is long in again assuming the color of its surroundings. The pulse in the larger arteries is reduced in volume or altogether wanting. A very characteristic symptom, and one which should be particularly noted, is the intermittent limp described by Charcot, probably depending upon anemia of the leg muscles. Following a rest of a few minutes the limb can be used as well as ever; the muscular cramp tending to return, however, after a short interval.

Gangrene nearly always begins in a toe, generally the great toe or the little one. Although it may appear spontaneously, it usually follows some comparatively trivial injury, such as a bruise, the wearing of an ill-fitting shoe, or the injudicious paring of a corn. The entire toe or a portion of it swells somewhat and becomes dusky red, purplish, and then bluish-black in color. As the toe dies, the pain, which is in most instances considerable, is transferred to the foot above. If infection does not occur the toe slowly dries into a hard, black, shrunken mass, or, in other words, becomes "mummified." But even when this takes place pus may form beneath the dry, black, tough skin, and burrow upward between the muscles. It is in such cases particularly that the gangrene extends more or less rapidly to the foot and even to the leg itself. This extension may occur without infection; but usually if bacteria can be kept out the gangrene remains dry, spreads slowly, and a line of demarcation is almost certain to form. This is usually situated at the base of a toe, but may be higher up; being regulated by the presence of infection, the character of the arterial obstruction, the resistance of the tissues, and the state of the collateral circulation.

Even though disease of the arteries exists upon both sides of the body, as it almost invariably does, the gangrene is nearly always unilateral, showing how much it depends upon local rather than general conditions.

Treatment.—Prophylaxis is of the utmost importance. When the symptoms indicate threatening gangrene complete rest should be enjoined and collateral circulation favored by elevating the foot and keeping it warm by wrapping it in cotton reinforced by a hot-water bag. Local and general circulatory stimulants are indicated, especially the local employment of electric baths, stimulating douches, and gentle friction with alcohol, soap liniment, or spirits of camphor. Gangrene can often be warded off in this way and sometimes indefinitely postponed.

When an affected toe is actually dead every effort should be made to keep it dry and prevent infection. After a preliminary cleaning and disinfection, wet dressings or poultices should not be used, but rather some antiseptic drying-powder, such as boric-acid powder, over which sterile cotton is applied somewhat loosely so as to permit evaporation. Under such management, or often without it, the process will limit itself to a single toe, a definite line of demarcation forming between it and the rest of the foot. It is wise not to be too precipitate in removing a toe of this character, because no matter how carefully the operation is performed it may lead to such extension of the gangrene as would require a much more serious amputation. In fact, it is frequently better to leave the dead member until it can practically be picked off without injury to adjacent living tissues, even though much time is required. While awaiting an appropriate time to operate, if the patient experience too much pain Bardescu advises section of the nerve supplying the part. Such a proceeding, however, can seldom be called for, because the administration of small doses of opium answers the same purpose and often seems favorably to influence the progress of the gangrene, especially in the presence of diabetes.

When the gangrenous process extends to the sole or dorsum of the foot, Haidenhain is probably correct in recommending immediate amputation, particularly if sepsis exists with burrowing of pus. His advice is to amputate in the lower portion of the thigh through tissues amply nourished by branches from the deep femoral, thus largely avoiding the danger of gangrene of the flaps which is apt to follow operations below the knee. This is quite generally recognized as the safer course; but nevertheless König and others prefer to remove the limb above or below the knee according to circumstances, the choice being made with reference to the general condition of the patient and the presence or absence of pulsation in the popliteal artery. Whichever situation is chosen, the result will depend much upon rigid asepsis and avoidance of unnecessary traumatism of the tissues.

There are those who operate under digital compression of the main artery rather than employ an Esmarch strap. This is done in order to avoid injury to the tissues and to calcareous vessels and to permit of testing the permeability of the artery in the wound; if blood does not flow freely when the compression is removed, a higher amputation is done at once. The necessity for this method is not generally admitted, however, particularly as a thrombus is usually quite easy to recognize, as it projects from the lumen of the main artery, without using the hemorrhage test. Some surgeons even advise against the use of sutures in uniting the flaps, the preference being given to adhesive strips and appropriate gauze pads.

The appearance of gangrene in a thigh stump, although always serious, does not necessarily mean disaster, as it may be limited in extent and comparatively harmless. In leg-stumps, however, it is of more importance and frequently requires another operation higher up.

The best time to perform amputation is a matter of careful judgment. To operate too soon may mean unnecessary loss of limb, while too great delay may result in still worse disaster. Furthermore it must not be lost sight of, although the question is difficult to estimate, that progress of the disease depends largely upon extension of arterial thrombosis, which blocks the collaterals as well as the main blood-channel. Therefore in pursuing a waiting policy too far thrombosis may so increase as to necessitate a thigh-amputation where an amputation below the knee would otherwise have sufficed. As a general rule, however, a line of demarcation should be well established before operation is resorted to.

Pre-senile, Spontaneous or Non-senile Gangrene.—This differs in no essential way from ordinary senile gangrene as described above, except that it occurs in middle-aged or young subjects. It also owes its origin to nodular arteriosclerosis, which, however, rarely develops into atheroma. Recent investigations have shown that this vascular disease is far more common in youth than was formerly supposed. The same prodromal symptoms present themselves as in senile mortification; such as disturbances in sensation, shooting pains, weak or absent pulsation in the arteries, muscular cramps, loss of function, cold and mottled skin, etc. They may exist to greater or less extent for months or even years before thrombosis finally shuts off the remnants of circulation and causes death of the part.

Like the senile form, the gangrene is apt to be dry; but infection may render it moist and result in burrowing of pus and rapid extension of the process. Similar rules apply in treatment.

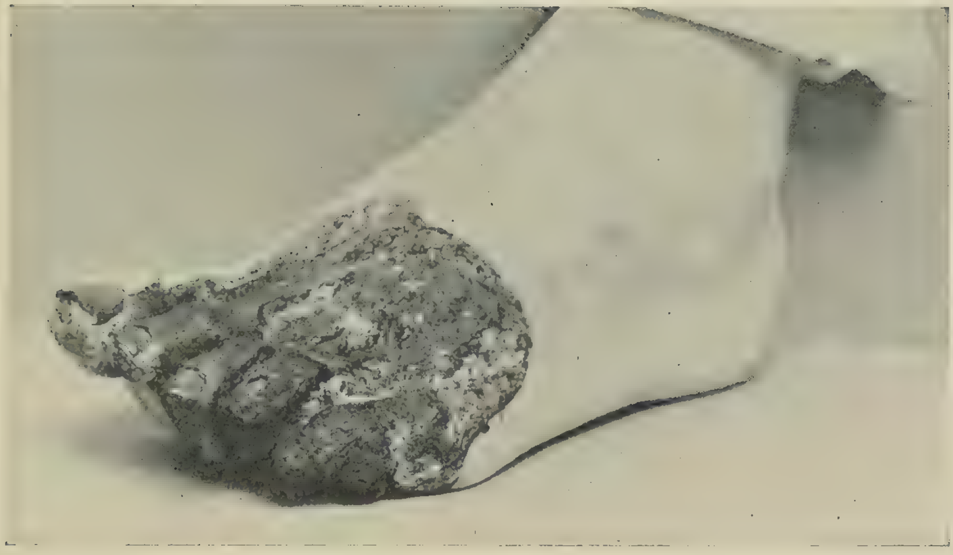
The term *spontaneous gangrene* has been much employed in describing this curious disease; but its more justifiable use is as a generic name covering all forms of mortification arising without an adequate external cause, such as senile and pre-senile gangrene, embolic, diabetic, and post-febrile gangrene, as well as gangrene from Raynaud's disease, lead, arsenic, mercury, syphilis, tobacco, leprosy, etc. In this connection it is perhaps well to emphasize the strong tendency of modern observers to recognize the dependence of all forms of so-called spontaneous gangrene upon alterations in the vascular coats, especially intima, thus discountenancing the theory of nervous origin.

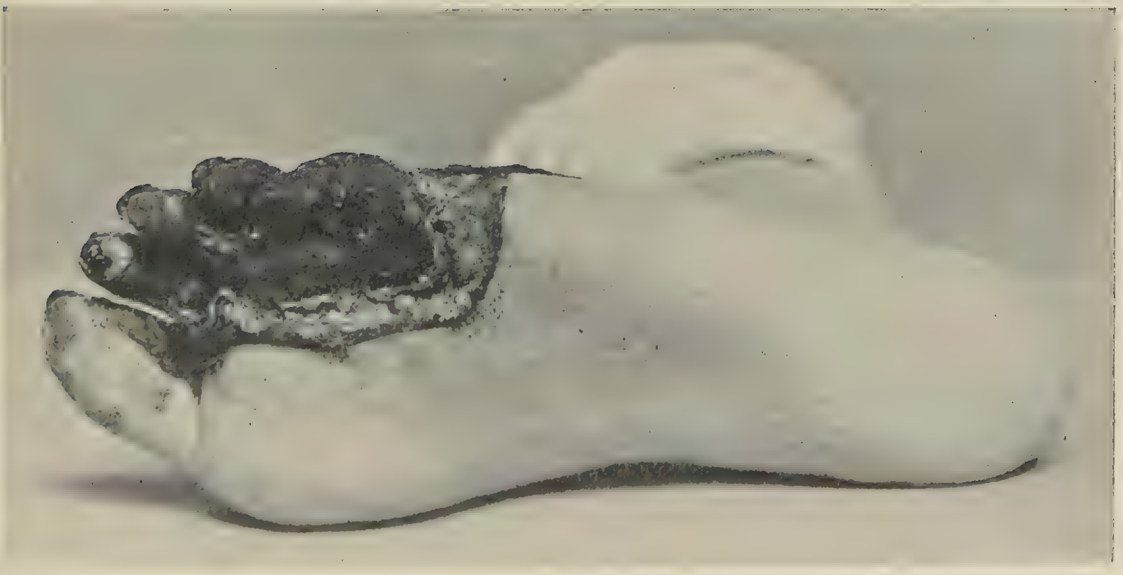
Diabetic Gangrene is a kind of spontaneous gangrene almost invariably referable to the same type as the senile and the pre-senile forms, and like them due to nodular arteriosclerosis complicated with thrombosis. Hence diabetes mellitus does not cause gangrene directly, as was formerly accepted without question; but it probably acts by favoring the development of arteriosclerosis, and predisposing to bacterial infection. Sugar in the tissues is peculiarly stimulating to the growth of microörganisms, consequently the poorly nourished and non-resisting tissues of a diabetic are unusually susceptible to traumatic or microbic mortification. By some, gangrene occurring in the presence of sugar is still referred to a peripheral neuritis, as taught by Auché, in 1892, arteriosclerosis being regarded as a mere coincidence.

Symptoms.—The prodromal and other symptoms are largely those of the varieties of spontaneous gangrene already described (see senile gangrene), modified, however, by the feeble capacity of the tissues to resist bacterial invasion. Infection, accompanied perhaps by general sepsis and suppuration, occurs readily and spreads rapidly, converting what would otherwise have been a dry process into a moist one. A line of demarcation is slow in forming, and even after it appears it may not mark the limit of the disease, which may travel beyond it.

The **treatment** is quite similar to that employed in senile and pre-

PLATE VIII*a*.





Diabetic Gangrene (Case of J. F. Binnie).

senile gangrene, except for the measures directed toward the diabetes itself, which should never be neglected. As long as the mortification is limited to a toe or a small area of skin it may be handled expectantly; but as soon as it shows a decided tendency to spread to the dorsum or sole of the foot, particularly if symptoms of severe infection are manifest, amputation should be strongly considered. Haidenhain advises always amputating in the lower third of the thigh irrespective of the extent of the necrotic process; while König and others operate either above or below the knee as circumstances may seem to demand, preferring occasionally to re-amputate rather than sacrifice too much in the beginning. Most surgeons follow the teachings of Haidenhain, believing that they lead to more definite and favorable results. Success in any case, however, depends much upon rigid asepsis, rapidity in operating, and avoidance of traumatism, and even then infection cannot always be prevented. Complicated methods should be avoided, drainage should be adequate, and sutures should not be tied tightly, or should be avoided altogether if possible. By some, digital compression of the main artery is preferred to the Esmarch strap. Absence of the patellar reflex is said by Reynier to contraindicate operation. Less stress is laid upon this sign, however, by others.

The amount of sugar in the urine seems to influence the operative results less than was formerly supposed, and this may also be said of the particular form of diabetes; but nevertheless it is well to amputate, other things being equal, when the percentage of sugar is as low as possible. On the other hand, the presence of acetone-bodies (acetone, diacetic acid, and beta-oxybutyric acid) is of the utmost importance, as they are responsible for the development of post-operative coma, which is frequently fatal and always to be feared, especially when oxybutyric acid is present in quantity (von Noorden). According to Kelly, symptoms will arise if acetone is present in greater amount than 0.02 gram in 50 c.c. of urine. To detect its presence he employs the following test: to 5 c.c. of urine, rendered alkaline with sodium hydrate, add a crystal of sodium nitroprussiate and shake well. Upon the addition of glacial acetic acid the foam becomes purple if acetone is present. Diacetic acid manifests itself by a Burgundy-red color when the urine, is treated with very dilute ferric chlorid. Ruff makes the statement that coma is to be feared as soon as the daily excretion of ammonia reaches 2 gm.

The existence of albumin in the urine seems to increase the danger of operation, although cases in which a large percentage is present often recover promptly. No amount of albumin or sugar should absolutely contraindicate surgical intervention, because advanced diabetic gangrene is almost necessarily fatal under any other form of treatment. They sometimes decrease in quantity or disappear after operation.

As a matter of interest it should be noted that following an injury, such as a fracture or a strangulated hernia, individuals who ordinarily present no sign of diabetes sometimes develop as high as 1 per cent. of sugar in the urine, without acetone bodies. This may last from one to ten days, and then completely disappear, never to return. The phenomenon was described as *ephemeral glycosuria* by Redard in 1886. A small amount of sugar in the urine, appearing in this transitory manner, could not influence to any appreciable extent the results of an operation; but it is of importance to the surgeon because there is no means of deciding that it does not represent a genuine diabetes. In such a case it is better to wait a few days before operating; or when this is impossible, to proceed as though genuine diabetes were really present (Krausch). Sugar may appear after general anesthesia, Röhricht having found it in twelve out of one hundred cases.

Owing to the danger of post-operative coma in diabetes (10.6 per cent., according to Ruff), which is often fatal, much importance is attached to the preparation of the patient and the method of anesthesia. Ether should be used instead of chloroform, because the latter more than the former seems to encourage the formation of acetone bodies, which are the real causes of disaster. As little anesthetic should be administered as possible, and never for diagnostic purposes alone if it can be avoided. The various forms of local anesthesia are preferable to general, but even these are not free from objection, owing to the danger of cutaneous necrosis and even coma. It is possible that spinal anesthesia may be of some service.

The preparation of the patient requires careful attention. The diet should, of course, be regulated as regards carbohydrates and fats. Food should not be withheld for too long a time either before or after operating, as starvation favors the formation of poisonous acids. Excessive purgation should be avoided. Sodium bicarbonate should be given in large doses, from 50 to 150 grams, until the urine becomes alkaline. It must be acknowledged, however, that the alkaline treatment is of more service in preventing coma than it is in counteracting it when once established, and that it is of somewhat doubtful utility at best. Nevertheless, the method should be tried in coma, pushing the alkali not only by the mouth, but also by the rectum, as well as subcutaneously and even intravenously. Karewski lays stress on the administration of large quantities of normal salt-solution by the bowel; and Kelley recommends the subcutaneous injection of a solution of adrenalin chlorid in a strength of 1 : 50,000—children being given 200 c.c. and adults 500 c.c.

Gangrene in Connection with Syphilis, Gout, or Bright's Disease differs but slightly from the senile, pre-senile, and diabetic forms; depending like them upon vascular changes and thrombosis together, perhaps, with weakened tissue-resistance.

Before operating in *albuminuric gangrene* the urinary function should be stimulated to the utmost by the administration of normal salt solution by the bowel; from four to eight ounces being injected every two to four hours until the desired result is obtained. Water should also be freely given by the mouth. Owing to the defective kidneys, local or spinal anesthesia may occasionally be preferable to chloroform or ether. In addition to the local prophylactic treatment already discussed under senile and diabetic mortification, special attention must be given to the affection of the kidneys. The rules governing operation are practically identical.

Raynaud's Gangrene (*Symmetric Gangrene of the Extremities*).— This is a form of spontaneous gangrene sometimes arising during the course of Raynaud's disease and supposed to be due to long-continued spasm of the smaller arteries. It occurs almost invariably in young adults, but cases in children and in those advanced in years are occasionally reported. Females are more susceptible than males, especially those who are neurotic or hysterical. The fingers or toes are the parts usually involved, although the trouble may extend to the feet, legs, or arms, and may rarely appear in the ears, nose, or even, it is claimed, in isolated patches upon the skin of the extremities or trunk.

Raynaud's disease, of which gangrene is merely an occasional ultimate result, is often described as a neurosis characterized by extreme excitability of the vasomotor centers. Pitres and Vaillard, whose views have not been widely accepted, ascribe it to a primary peripheral neuritis. In consequence of some comparatively trivial cause, or apparently without any, the arterioles of a finger or toe are stimulated to such strong contraction that the circulation is more or less completely cut off, and if this persist long enough, gangrene results. A fit of passion or other excitement may be sufficient to produce the phenomenon, or it may be due to reflex irritation from a diseased uterus, stomach, or other organ; but in the majority of instances it arises from the effects of cold, even of very moderate degree, the symptoms closely resembling those of frostbite, although the tissues are not frozen. Hence it is more frequently seen in winter than in summer.

Theoretically the disease as described by Raynaud should invariably be symmetric, attacking both hands or both feet, or even the four extremities together; but practically this is not always true. One or more fingers or toes, which have previously been subject to tingling, itching, and pain, suddenly become as cold, white, and motionless as if dead or frozen (so-called "dead-fingers"). The condition is accompanied by burning or lancinating pain, in spite of anesthesia of the skin, and is known as *local asphyxia*. Instead of becoming anemic the finger may be passively congested, swollen and painful; presenting a bluish, mottled, or purplish appearance, as though constricted at its base. This latter condition often succeeds the former or alternates with it in limited areas. It is called *local syncope*. If recovery result without gangrene, the syncope soon gives way to active congestion, the finger becoming intensely hot, red, and painful. This process may be repeated indefinitely, at longer or shorter intervals, sometimes months or even years apart, without resulting in mortification, even though the discolored skin so nearly succumbs as to become covered with vesicles during the attacks. When gangrene does result, although occasionally severe, it is apt to be of a mild type, involving small areas of skin only, even when an entire finger or hand has seemed doomed to destruction. In this way ulcerations of the ends of the fingers are produced, resulting in white scars, contracting fibrous tissue, and loss of the nails; a condition designated as *sclerodactylus* (even scleroderma itself is regarded by some as a form of Raynaud's disease). The end of the nose or portions of the rims of the ears may thus be lost. Carl Beck has demonstrated with the Roentgen ray that the bones may be affected as well as the superimposed soft parts.

Many cases described as Raynaud's gangrene have undoubtedly been instances of senile, pre-senile, or diabetic gangrene. In fact, with the increase of knowledge regarding the relation of spontaneous mortification to changes in the vascular coats, instances of Raynaud's gangrene are becoming correspondingly rare. Nevertheless cases occasionally arise in which vascular changes cannot be demonstrated, especially in the hysterical. It should not be lost sight of, however, that symmetric nodular arteriosclerosis is much more common in the young than was formerly supposed, and that it may be confined to small areas of the vascular intima, thus making it difficult to detect. (See pre-senile and senile gangrene.) Arterial spasm acting upon such a basis in conjunction with thrombosis might easily produce mortification; but it is difficult to comprehend how spasm alone could be protracted enough to do this. Nutritive vascular changes from anemia consequent upon repeated and prolonged arterial contraction, or arteritis depending on toxic substances in the blood, could be of material assistance in the process. In this connection it is of interest to note the similarity of the premonitory symptoms of Raynaud's disease to those of senile and pre-senile gangrene.

Prophylaxis and treatment differ in no way from that employed in senile and pre-senile gangrene.

Gangrene from Ergot arises almost invariably from eating bread made from "spurred rye," and very seldom if ever when the drug is taken for medicinal purposes. In former times, especially in Europe, during unfavorable harvests the heads of rye sometimes became infected with the fungus of ergot (claviceps purpurea), and epidemics of ergotism resulted. Occasionally as high as 10 per cent. of the meal consisted of ergot. One of the last epidemics of this kind occurred in Flanders and Burgundy in 1816. At present the disease is seldom met with, and then sporadically only. In America it is very rarely seen. It deserves consideration more from its past importance than for its present interest.

Ergotism sometimes exerts its greatest influence upon the nervous system and sometimes upon the vascular. In the former instance the *convulsive* type results and in the latter the *gangrenous.* Not infrequently these types are more or less combined.

The first **symptoms of ergotism** appear in connection with the gastro-intestinal canal, in the shape of chronic diarrhea, colic, vomiting, etc. These are closely followed by disorders of vision, dizziness and headache, and disturbances of the circulatory and nervous systems, resulting in numbness, coldness, blueness, tingling, itching, pain, and weakened pulse in the extremities, with frequent muscular spasms. These spasms may become general and even eventuate in convulsions or epileptiform seizures (convulsive form). In cases terminating in gangrene, the local symptoms are pronounced, particularly those connected with a deficient supply of blood. It is usually the toes rather than the fingers which are affected. They become cold and mottled and the seat of considerable pain. Presently a purplish spot appears, which extends in size until the toe, and possibly the foot, or rarely the whole extremity as far as the hip, becomes the seat of a gangrene which is usually dry, but may be moist, particularly in the presence of infection. A well-defined line of demarcation forms in the great majority of cases. Occasionally a patient will lose an ear or a portion of the nose from mortification.

Gangrene from ergot bears a very close resemblance to senile and other forms of spontaneous gangrene both in its symptoms and its pathology. In it have likewise been found degeneration of the vascular intima accompanied by thrombosis, due in all probability to the effects in the circulation of sphacelinic acid, a constituent of ergot. A theory of causation, which has been quite generally accepted, is that the death of the tissues is caused by deprivation of nutrition due to prolonged contracture of the smaller vessels (Holmes). That such vascular spasm is a characteristic feature of ergotism cannot be doubted, but that it is solely responsible for the production of gangrene is open to question.

Treatment.—The principal features are, to be sure that the patient ceases to receive ergot into the system, and to hasten the removal of that which is already present by purgatives and other eliminants. Threatened gangrene should be combated, as in the senile form, by warmth and general circulatory stimulants, such as alcohol, coffee, and nitroglycerin; and by local stimulating baths, careful massage, and friction. Amputation is of course indicated when gangrene is fully developed, but a line of demarcation should first become thoroughly established. The rules governing operation are similar to those in senile and pre-senile gangrene.

Gangrene from Frostbite.—The motionless unclothed body remains in normal condition at about 98.4° F., in a dry, quiet atmosphere. To comfortably withstand lower temperatures clothes or exercise are necessary, and then –40° F. to –60° F., and even much colder, may be borne with impunity. A great deal depends, however, upon habit and the suddenness with which changes in the temperature occur. Unconsciousness is said to supervene in about ten minutes if an individual remain perfectly quiet and naked at about 10° F. (Hildebrand). When the air is damp or in motion susceptibility to cold is much greater.

Both general and local effects are produced by cold. The former, which often precede the latter, manifest themselves in congestion of internal organs, with stupidity, lassitude, and an intense desire to sleep. The wanderings of one who is lost in a blizzard, for instance, are finally checked by a feeling of unutterable weariness and exhaustion and an almost uncontrollable tendency to lie down and rest. If this is yielded to, unconsciousness soon supervenes, followed by freezing of portions of the body, or even death itself if help is not forthcoming. The danger is especially great in those of low resisting power—in the old and in the young, and in individuals debilitated by hunger, sickness, or the excessive use of alcohol. Most cases of frostbite treated in hospitals occur in alcoholics who have lain out overnight in a drunken stupor. Even a moderate use of alcohol is said by arctic explorers to increase the liability to injury from cold.

Dry cold is much better borne than when moisture is present in the atmosphere; and if the clothing or feet are wet, the likelihood of freezing is still further increased, especially if the wind is blowing. The parts most frequently affected are the feet and the hands, particularly the toes and fingers, together with the nose, ears, chin, and cheeks; not altogether because the peripheral circulation is feeble in the extremities, but also because they are more exposed and the cold can get at them from all sides, thus extracting heat more rapidly. Rarely the male genital organs are frozen. Tight shoes or gloves increase the susceptibility by lessening the supply of blood.

The first effect of cold is stimulating. The circulation is increased, causing redness of the skin; but as the point of toleration is passed, anemia with intense paleness suddenly develops, due to spasm of the smaller arteries. Tingling, numbness, and pain are felt, often severely, but all sensation disappears when the parts become actually frozen. As freezing progresses complete stasis develops, leaving the tissues filled with venous blood which gives to them a dark red or bluish tinge. Swelling takes place in a short time, and blisters form upon the surface, filled with serum dark with blood-pigment from disorganized red corpuscles. Beneath these blisters is usually a necrotic area of cuticle which can be seen when the vesicle is broken.

From these lighter degrees of frostbite recovery takes place completely or with trifling losses of skin, although the pain is considerable both at the time of freezing and during the process of thawing. Sometimes, however, more or less permanent damage is done to the blood-vessels; resulting in disfiguring hyperemia, for instance, of the end of the nose. Lasting changes in the nutrition of the tissues may arise, causing the development, especially about the hands and feet, of discolored and sensitive, infiltrated patches known as *chilblains* or *pernio.*

When the freezing is more decided, still greater damage is done. The skin, deprived of its vitality, becomes livid and then brownish, and in the course of time black. Not only the cuticular covering, but a toe or a finger or an entire limb may perish in this way, the muscles becoming opaque, grayish, and friable. The gangrene is generally of the dry variety, but is sometimes moist. The former is said to result when the arterial blood is completely shut off before reactive inflammation sets in; while the latter is due to inflammatory changes while there is still a little circulation left. Unless complicated by severe bacterial infection, which is seldom, a distinct line of demarcation ultimately forms; and if the process is undisturbed by operative measures the dead portions gradually separate and drop off, leaving more or less firmly cicatrized surfaces, which are often sensitive and ulcerate easily. As the tendons and bones disintegrate last, the patient sometimes presents the startling phenomenon of being able to move toes or fingers long after they have perished.

For the sake of convenience it is customary, as in burns, to divide frostbites into three degrees according to severity, although no sharp lines can be drawn between the different kinds. The *first degree* is a transitory erythema, usually disappearing rapidly, but possibly causing more or less permanent vascular changes (chilblains, etc.). In the *second* *degree* blisters form, beneath which necrotic areas of skin often exist in which ulcers sometimes develop. In the *third degree* the parts are so badly frozen that extensive gangrene results.

Gangrene from frostbite differs in no essential from other forms of mortification; but the manner of its production has peculiarities worthy of consideration, although the exact pathology is still obscure. It is reasonably certain, however, that death of the tissues occurs in two ways: (1) from direct action of cold upon the protoplasm of the cells (Rischler), and (2) from ischemia due to vascular spasm and thrombosis, the latter being a much more prominent factor than the former. It is doubtful if the nerves have anything to do with the process, although degenerative changes have frequently been seen in them. It can be said, in fact, that gangrene is usually due to the cutting off of nutrition by vascular obliteration from tissues which are already damaged by freezing. But it must be understood that parts may be frozen through and through, so that the blood and all other fluids are converted into ice, and remain so until their vitality is destroyed. In most instances, however, there would be a chance for life to be retained if it were not for the occurrence of thrombosis, arterial or venous or both. This is due to injury of the internal coats of the vessels by cold and deprivation of nutrition owing to stagnation or freezing of the blood. These vascular lesions are sometimes described as arteritis (Ruduitski) and sometimes as hyaline degeneration (Kriege and von Recklinghausen); but whichever they are, the effect is the same—roughening of the intima and deposition of clots, either hyaline or fibrous. The changes in the vessels, although they may not cause gangrene, are sometimes permanent and give rise to chilblains, ulcers, and other disturbances of nutrition.

Extensive exudation into the tissues occurs, provided the vitality of the part has not been absolutely destroyed. It is practically identical with that observed in inflammatory conditions. Ordinarily this is probably of service in the process of repair; but when it is excessive and of too sudden occurrence so much pressure may be exerted upon the smaller vessels that retardation of circulation and encouragement of thrombosis may result from this source alone. Hence the wisdom of thawing out a frozen extremity rather slowly instead of too rapidly, combined with the use of elevation and gentle friction and massage in order to encourage the exit as well as the entrance of fluids. The presence of an excessive quantity of exudate and its escape beneath the epithelium accounts for the upheaval of vesicles and blisters. It also explains the occurrence of moist gangrene, which is said not to appear unless sufficient vitality remain in the part to permit of circulation and exudation.

In a few words, then, the phenomena following freezing arise from (1) direct damage of the tissues, (2) exaggerated inflammatory reaction, (3) degenerative changes in the vessels, and (4) the formation of thrombi, which are usually the cause of gangrene. Hence the mortification of frostbite resembles senile and pre-senile gangrene in its causation, appearance, and course, the chief difference lying in the acuteness of the vascular changes.

Treatment.—Reaction should be brought on slowly, in order to avoid the severe pain accompanying a too rapid return of the circulation, and also to prevent the gangrene which may result from sudden exudative engorgement of the tissues. This is a view which has existed for hundreds of years and is still held today by the laity and by nearly all practitioners. It has the support of a vast amount of clinical observation, accumulated principally in military practice. Recently, however, Ritter and others, following the teachings of Bier, have advocated exactly opposite treatment, namely, the use of superheated air by means of hot-air ovens. Basing their assertions upon experiments on dogs, they claim that the results are superior to those obtained by the older method; but in spite of this, their ideas have not yet been generally adopted. The treatment may be tried, however, with impunity in the chronic forms of frostbite, such as chilblains, ulcers, etc., where it is said to accomplish much in a short space of time. The oven should be used daily for from one-half to one hour during the course of from three to ten days. The same favorable results are said to be obtained by elastic constriction used according to Bier, which produces a passive hyperemia of the extremity.

The almost universally accepted treatment of acute frostbite is to place the patient in a cool room and gently rub the frozen part with snow or with cloths wrung out of ice-water, taking care not to injure the skin for fear of subsequent infection in case gangrene develop. Gradually the temperature of the water and of the room may be increased, and the warm bare hands used instead of cold cloths. When the circulation has been fully restored, where restoration is possible, the part should be slightly elevated, to encourage venous and lymphatic drainage, and wrapped in cotton. If mortification is imminent, or if extensive blistering has developed, the skin, as in a burn, should be rendered as clean as possible and an aseptic dressing applied in order to ward off infection. Dryness, which is a great protection against bacterial invasion, should be aided by the liberal use of antiseptic dusting-powders, such as boric acid.

Owing to the difficulty in determining the extent of gangrene in frostbite, the rule is not to amputate until a distinct line of demarcation has formed. Even then it is better not to be too precipitate; because what seems like complete death of a part may be necrosis of skin only, which a skin-grafting operation might remedy later on. By pursuing a waiting policy dead portions of fingers or toes may often be picked off at a joint or nipped off with bone-forceps without resorting to formal amputation, thus permitting valuable parts of fingers to be saved which would otherwise be sacrificed. In observing this rule, however, it must not be overlooked that moist gangrene requires prompt action when it shows a tendency to spread.

The treatment of the general effects of cold should be governed by the same principles as those employed in local freezings. The patient should be placed in a cold room the temperature of which is slowly elevated, in order to lessen the danger of congestion of internal organs. Stimulation must be cautious and gradual, and accompanied by careful rubbing of the body, first with cold wet cloths and then with the bare hands. Some advise immersing the patient in a cold bath to which warm water is slowly added; but such treatment should be employed with reservation, to say the least. Efforts at resuscitation should not be given up too soon, for patients have been revived after remaining several hours in an apparently hopeless condition.

Embolic Gangrene is caused by arterial obstruction from emboli. These usually originate in the left side of the heart, although they may come from other sources, such as an atheromatous aorta or the discharge of a tuberculous focus into the circulation. Emboli starting from the right side of the heart may give rise to gangrene of the lung. A foreign body traveling in the blood lodges in most instances at the bifurcation of an arterial trunk, as in the upper calf, or below the elbow. The obstruction is usually partial at first, but is soon rendered complete by secondary thrombosis, which is also apt to close the mouths of collateral vessels, thus leading to gangrene. If the collaterals escape, mortification is not apt to occur. The presence of arteriosclerosis can materially aid in the process.

The secondary thrombosis is sometimes very extensive. In embolism of the popliteal, for instance, it may travel upward through the femoral into the iliacs, and even across the bifurcation of the aorta to the vessels of the other side, thus causing gangrene of the opposite extremity.

From what has been said it will be appreciated that in most instances embolic gangrene is really gangrene from thrombosis, thus resembling closely the senile type in its pathology.

Symptoms.—The onset is rapid and without prodromata except on the part of the heart. A sudden and severe pain is felt at the bifurcation of a large artery, say, the popliteal. This is followed by obliteration of the pulse together with coldness and lividity of the extremity, although these symptoms may be delayed until thrombosis occurs. Occasionally the artery can be felt as a firm tender cord rolling under the finger. The resulting mortification is in the majority of instances dry; but it may be moist, provided sufficient collateral circulation remains to fill the tissues with blood without providing enough propulsive power to drive it out again through the veins. More than one extremity, and occasionally all of them, may be affected at the same or at different times.

The **prognosis** is in most instances unfavorable owing to the danger of further trouble from persisting cardiac complications, and also from the fact that arteriosclerosis is frequently present.

The **treatment** is identical with that of senile gangrene. Anesthetics are usually well borne in spite of the disease of the heart, provided compensation is reasonably good. It may be necessary to perform several synchronous or consecutive amputations on the same patient.

Post-febrile Gangrene.—Mortification is occasionally observed as a dreaded and disastrous complication of typhoid and typhus fevers, smallpox, scarlatina, diphtheria, measles, whooping-cough, erysipelas, cholera, puerperal fever, bubonic plague, etc. It is more frequent in typhoid, however, than in any of the others. In measles the mouth and cheeks are particularly susceptible (noma); in scarlatina, the neck and parotid regions; in variola, the pharynx and cartilages of the larynx; and in typhoid, the lower extremities. Males, for some reason, seem to be more often attacked than females.

In all instances the gangrene is due to obstruction of the circulation by thrombosis; generally of the arteries, occasionally of the veins, and sometimes of both. The thrombi arise because of changes in the vascular intima; depending upon toxins circulating in the blood, defective nutrition, or occasionally upon local bacterial growth. They rarely have their origin in cardiac emboli which have lodged at some vascular bifurcation, or in colonies of germs which obstruct the lumen of a vessel by excess of numbers alone. As factors of more or less importance may be mentioned debility and loss of resistance from long-continued or severe fever; feebleness of circulation; uncleanliness, particularly as regards urine and feces; bad hygienic surroundings; poor food and nursing; and possibly great mental depression. The resemblance between post-febrile and other forms of spontaneous gangrene, such as senile, pre-senile, diabetic, etc., is very striking, the main difference lying in the acuteness of the vascular changes.

Other things being equal, gangrene is more apt to occur in the more severe cases of fever; but nevertheless it is at times unexpectedly met with in the milder forms. Whether it is dry or moist varies with the location and character of the vascular thrombosis and the advent of subsequent infection. In the extremities the process is usually dry, owing to plugging of an artery; although it may be moist in case there is infection or venous obliteration. About the trunk, genitals, and face the gangrene is nearly always moist; for instance, in noma. Sometimes the two forms exist side by side; or the moist will supervene upon the dry if infection occur.

Much surgical interest centers about *typhoid gangrene*, because of its comparative frequency and the attention called to it by the writings of Keen in this country and various others abroad. Although formerly common, especially in epidemics among soldiers, it is at present rarely met with. It is seen more frequently in severe typhoids, generally making its appearance in the second or third week and seldom later than the sixth or seventh week. It attacks by preference the lower extremities, although it is sometimes observed in connection with the nose, ears, face, genitalia, perineum, anus, and skin of the trunk. Internal organs are rarely involved. All ages are apt to suffer, but males are more susceptible than females in the proportion of three to two.

When an extremity is affected the symptoms are quite characteristic. In a case of typhoid which seems to be progressing favorably, severe pain will occur, for instance, in the leg, from sudden thrombosis of a large artery. It is accompanied by coldness, numbness, and pallor of the parts below, followed by discoloration of the skin and the usual phenomena of dry gangrene. Or, without especial discomfort outside of numbness and disturbances of sensation, the nose, ears, genitals, or other portions of the cuticle will become bluish, and finally black and gangrenous, due to thrombosis of the smaller vessels. In this way a finger, a toe, a leg, portions of the ears or nose, or even a large part of the face may perish, causing the most horrible disfigurement. Large areas of skin covering the abdominal or chest walls or the genitalia may slough away.

Treatment.—Of more importance than the treatment of typhoid gangrene is its prevention; by careful nursing, good hygienic surroundings, and attention to diet and stimulation, in mild cases as well as severe ones. Local injuries should be avoided in the course of handling or bathing the patient, and minute and frequent examinations should be made of every portion of the body, in order that no incipient trouble escape notice. Threatened gangrene of an extremity must be met with moderate elevation and gentle friction and massage, combined with hot and cold baths and douches and electrical applications; protecting the part between these procedures by wrapping it in cotton reinforced by bags of warm water if necessary. General stimulation is also indicated. When gangrene appears the part should be rendered as aseptic as possible and maintained in this condition by appropriate dressings, which must be loose and so arranged as to favor evaporation. In the majority of instances amputation should not be performed until a well-marked line of demarcation appears; and even further delay may be indicated provided the patient's condition contra-indicate immediate operation. Moist gangrene demands more prompt attention than dry, especially if decided symptoms of general sepsis exist. Spreading gangrene of the face or elsewhere, as in noma, may require the actual cautery. (See chapter on "The Surgical Complications and Sequels of Acute Infectious Disorders.")

Bedsores or Decubitus.—An annoying and often serious complication arising during the course of protracted and severe forms of illness is the development of bedsores. These areas of cuticular necrosis appear in the great majority of instances upon dependent portions of the body where the soft parts are subjected to long-continued pressure between the bed and some more or less superficial bone; for instance, over the sacrum, the trochanters, the scapula, the spinous processes of the vertebræ, the external malleoli, the heels, and the internal condyles of the humerus. When, however, the tissues are very susceptible, bedsores may appear upon any portion of the body, even if the pressure is slight or transient, such as is produced by the mere weight of the bedclothes or of a hand lying upon the abdomen. In cases of extreme emaciation certain bones, particularly the anterior superior spinous processes of the ilium, may protrude through the overstretched and atrophic skin without the aid of external pressure at all. In special instances the mere resting of one cutaneous surface against another, for instance, about the vulva or scrotum, may cause death of the tissues, particularly if there is contamination by feces or urine.

Decubitus is most frequently encountered in severe and lasting fevers accompanied by emaciation and prostration, such as typhoid and osteomyelitis. It is also seen in diabetes, Bright's disease and other affections accompanied by vitiated conditions of the blood, and in certain lesions of the central nervous system, especially those giving rise to paralysis. Severe injuries of the spinal cord or peripheral nerves are extremely liable to be complicated by the most sudden, extensive, and troublesome bedsores.

In considering the **causation of bedsores** it is customary to keep prominently in view their division into ordinary decubitus and that appearing in connection with nervous lesions, although it is doubtful if any real difference exists between them. Both varieties probably originate in thrombosis of the smaller vessels, which gives rise to gangrene, sloughing, and ulceration, extending more or less rapidly and extensively according to the resisting power of the tissues.

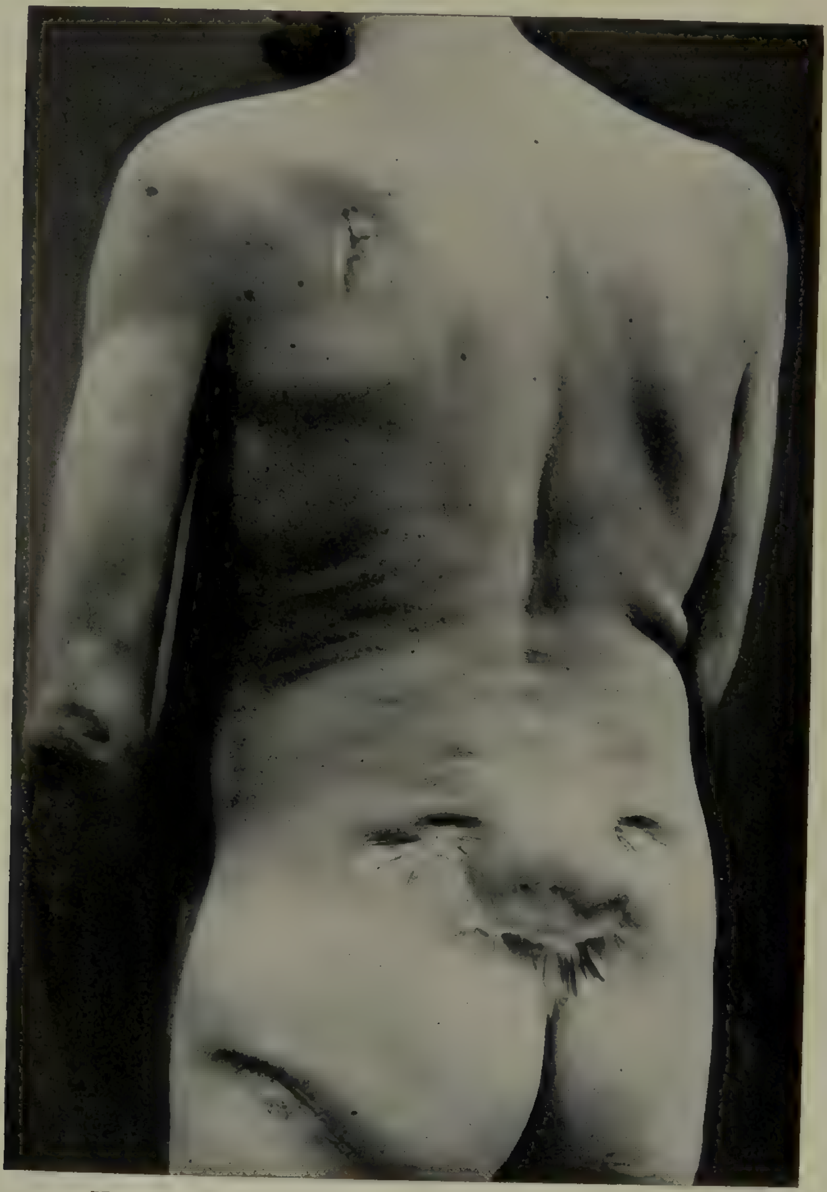


FIG. 77.—SCARS OF HEALED BEDSORES ON THE SHOULDERS, ELBOWS, SACRUM, POSTERIOR SPINE OF THE ILIA AND GREAT TROCHANTERS AFTER TYPHOID FEVER (Keen).

In *ordinary bedsores* the thrombosis is due to a variety of causes; the most prominent being pressure, aided by the disappearance of the normal protecting and elastic layer of fat. Pressure alone, however, is not sufficient, as is demonstrated by the fact that patients may lie in bed for years without ill effects as far as injury to the skin is concerned. Other factors of greater or less importance are (1) hypostasis, upon which Unna lays so much stress, which arises from feeble circulation in the undermost portions of the body; (2) lack of tissue resistance, caused by disease, weakness, and defective metabolism; (3) alterations in the vascular intima, due to bacterial poisons, lack of nutrition from capillary stasis, changes in the blood, etc., and (4) evaporation of fluids from the tissues, which takes place, according to Unna, in the presence of anemia when the adipose tissue has vanished and the protecting epithelium has been rubbed off, as it often is against the coverings of the bed.

The decubitus accompanying lesions of the nervous system differs from the ordinary form in no way except in its amazing rapidity and destructiveness. Charcot and others have attempted to explain these peculiarities of "acute bedsores" by assuming the existence of certain trophic centers governing nutrition, damage to which results in "neurotic necrosis" when aided by local pressure. These trophic centers have never been demonstrated, however, with certainty. It seems equally plausible that the phenomena are due to thrombosis depending upon nutritive alterations in the vascular intima which in their turn arise from capillary stasis originating in injury to the vasomotor nerves or centers. This theory, to say the least, is more in accordance with the principles of the causation of gangrene in general.

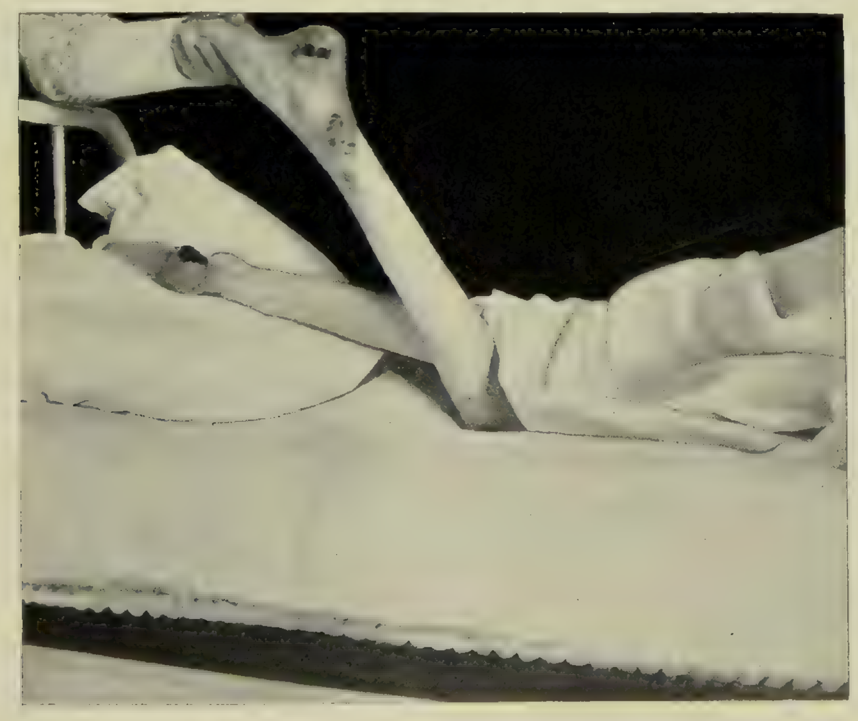


FIG. 78.—DECUBITUS OF BOTH FEET FROM TYPHOID FEVER.

The presence of bacterial infection, which always occurs sooner or later, adds greatly to the virulence of a bedsore, causing ulceration and retarding the process of healing. Other external agents are—soiling with feces or urine; irregularities of the bedclothes or the presence of crumbs; maceration of the skin from perspiration; injury from rough handling, splints, hot-water bottles, tight bandages, etc. And it must never be lost sight of that the application to incipient bedsores of compresses wet with solutions of carbolic acid may lead to increased disaster by action of the drug upon the already devitalized tissues.

Symptoms.—Bedsores begin with passive hyperemia of the skin, manifesting itself in a dusky-red color. This is followed by a purplish tinge, gradually becoming black as gangrene develops. Bacterial infection soon takes place and is succeeded by inflammation and ulceration. The surrounding tissues become red, and swollen from exudation, pus being plentifully secreted. When the gangrenous sloughs separate, a ragged unhealthy ulcer is exposed. This may remain small in size; but it often extends rapidly in circumference and depth, causing frightful loss of tissue. Not infrequently the underlying bone is exposed, and when the sore occupies the sacral region it may eat into the spinal canal itself. Death can occur from exhaustion, sepsis, pyemia, or spinal meningitis. If recovery take place disfiguring cicatrices are apt to form, which are occasionally so extensive as even to interfere with locomotion.

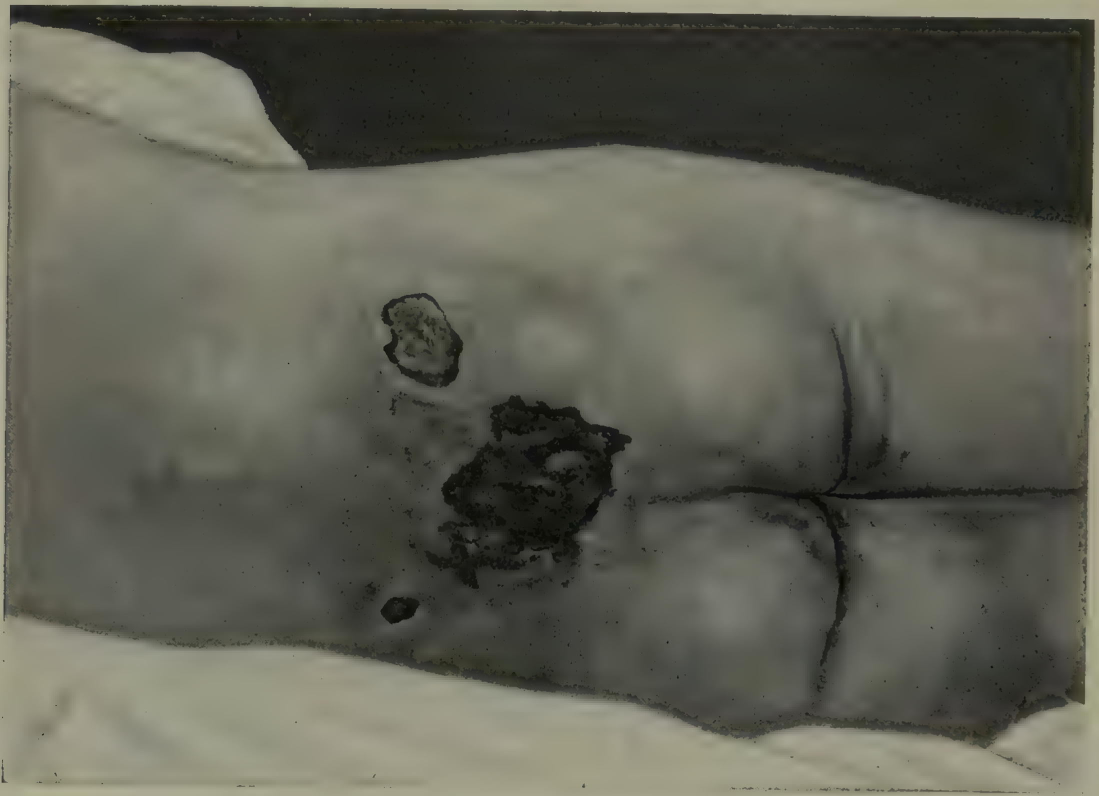


FIG. 79.—BEDSORES FOLLOWING MYELITIS.

Ordinary decubitus is usually of slow formation; but the neurotic form appears with astounding rapidity, a few days or even hours being sufficient for the production of large necrotic areas, even upon portions of the body exposed to only trivial pressure. There is no pain in the latter variety, owing to the presence of cutaneous anesthesia; but in the former the suffering is often intense, especially after ulceration appears, provided the patient's senses are not too obtunded by disease.

The healing of a bedsore is naturally slow in spite of all treatment, owing to the weakened condition of the tissues. It often does not take place at all until the disease which caused it has subsided, or the injury to the spinal cord or peripheral nerve has undergone repair. Hence they may exist for weeks, months, or even years; giving rise to necrosis of bone and tendons, and possibly to amyloid degeneration of internal organs from long-continued suppuration.

Treatment.—Prophylaxis is the first consideration; although when lesions of the nervous system exist, especially a crush of the cord, bedsores are almost certain to appear sooner or later in spite of the most scrupulous care. In hemiplegia the paralyzed parts should be protected by the patient lying upon the sound side as much as practicable.

Wherever the possibility of the development of decubitus exists, the skin of the vulnerable parts should be kept *clean, dry,* and *free from pressure.* Once or twice daily, or oftener if demanded by soiling with urine or feces, the back should be gently washed with soap and water, exercising great care not to injure the tender surface for fear of infection, and then thoroughly dried, and dusted with borated talcum powder. Applications of a solution of 8 to 15 grains of alum to Oj of 50 per cent. alcohol are of much service in cleaning the skin and hardening its surface. Spirits of camphor, vinegar, lemon-juice, or salt-and-whisky (ʒij to Oj) are frequently used for the same purpose. Sheets should be changed often, if for no other reason than to prevent the decomposition of perspiration; and they should be kept tightly stretched across the bed by pinning them to the mattress, in order to avoid wrinkles. Irritating substances such as crumbs should be guarded against, and the position of the patient changed as often and as completely as the exigencies of the case will permit.

Soiling with urine and feces must be promptly attended to, and it may be necessary to protect the exposed portions of the body with a powder of stearate of zinc or with boric acid or zinc ointment. In vesical incontinence in male patients the use of some sort of permanent urinal is imperative. When necrosis of the skin is imminent the employment of collodion or other substances is frequently advised as a protection; but their utility is doubtful, because they prevent the giving of proper attention to the cutaneous surface.

In most instances pressure may be relieved by the employment of pneumatic rubber rings covered with cloth, or by rings made from rolls of cotton, which are placed beneath the pelvis and the heels. In bad cases, however, such as a fracture of the spine, it is better to put the patient at once upon a pneumatic bed or water-bed, being careful not to render it too resisting by overfilling. Pads of cotton directly beneath the vulnerable points are worse than useless, because they add to the pressure which already exists.

When gangrene has occurred the ulcer must be treated antiseptically in addition to relief of pressure. Sloughs are to be clipped away, using care not to injure the living tissues, collections of pus opened, and the sore and its vicinity washed with an antiseptic solution. Dusting-powders can often be used to advantage, such as stearate of zinc, iodoform, boric acid, aristol, etc., and an aseptic absorbent dressing applied.

Sometimes, however, compresses wet with hydrogen peroxid, mild solutions of boric acid or bichlorid of mercury, or perhaps a boric acid or zinc ointment are more effective than dry dressings. Often the application of pure bovinine on patent lint will be most effective in healing a bedsore. If stimulation is indicated, a salve composed of Argent. nitric., 1. 0; Bal. Peruvian , 10.0; and Ung. zinc. oxid. ad 100.0, is quite satisfactory. Stimulation may also be obtained by the employment of ice-cold compresses for a few minutes, followed by hot applications (Keen); and both stimulation and disinfection result from lightly searing the surface with a stick of lunar caustic or with pure carbolic acid.

In extremely bad cases accompanied by great suffering the continuous bath should be used when possible; the body of the patient being fully immersed in a tub of water, which is kept clean by continuous overflow and renewal, and at a constant temperature by an appropriately arranged thermostat. A tub of this character should exist in every well-appointed hospital. Perfect drainage and relief from pressure are thus secured, and the comfort and chances for recovery of the individual vastly augmented. Unfortunately, however, this treatment is seldom practicable when it is most needed; for instance, in recent fractures of the vertebræ.

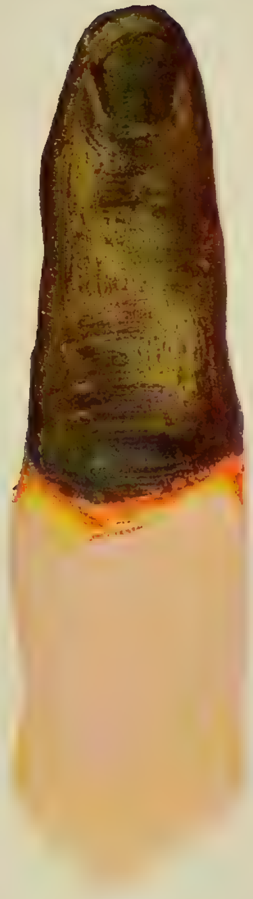
Carbolic-acid Gangrene.—Within recent years attention has been strongly called to the fact that weak aqueous solutions of carbolic acid may cause gangrene when continuously applied to the skin, particularly of the fingers and toes. In 1899 Harrington reported 18 cases occurring within five years in the Massachusetts General Hospital, and collected 132 published cases. Lévai found 26 cases among 20,417 patients in the General Hospital for Workmen, in Budapest. Undoubtedly, however, it is much more common than would appear from the literature, as there can be no question that the majority of cases remain unrecorded.

In injuries and inflammations of the toes and fingers it is the habit of many who are not physicians, and unfortunately of some who are, to wrap the parts in compresses soaked with solutions of carbolic acid. The effect of this is to produce gangrene in a few cases, but by no means in all. There is primarily some tingling and numbness, such as every surgeon has experienced after immersion of the hands in carbolic solutions, but soon all sensation disappears. The skin is at first white; afterward turning yellowish, brownish, and grayish-black or black. The skin alone may be affected; but if the process continue, an entire toe or finger may become hard, shriveled, and gangrenous.

Weak solutions of other chemicals, such as lysol, the mineral acids, acetic acid, and potassium and sodium hydrate, are capable of producing similar effects when applied for a sufficiently long time (Lévai). I have seen complete gangrene of the two terminal phalanges of an index-finger result from the use of compresses wet with "campho-phenique." It should also be mentioned in this connection that orthoform alone, or in combination, occasionally produces gangrene when applied to ulcerating surfaces.

The difficulty is usually produced by solutions varying in strength from 3 per cent. to 5 per cent.; but sometimes by 2 per cent. solutions and even

PLATE IX.



CARBOLIC GANGRENE.

Appearance of a finger four weeks after the application for twenty-four hours of a dilute solution of carbolic acid. The finger was wrapped in cloths which were saturated with the carbolic solution not stronger than five per cent. Amputation necessary. Inflammatory process at the base of the finger shown by the reddened tissues (Harrington's case).

those as weak as 1 per cent. Strong carbolic acid is not so likely to produce gangrene, although it sometimes does, because a tough layer of necrotic tissue is immediately formed, which prevents penetration of the acid to the underlying tissues; while the weaker, watery solutions soak through the macerated epidermis with comparatively little hindrance. It is only when the dressings are kept moist and remain in place for a number of hours, usually twelve to forty-eight, that disaster results, and then in a few cases only, most skins seeming to offer an adequate resistance.

In endeavoring to account for the phenomenon, several theories have been advanced: (1) that all of the carbolic acid fails to dissolve, the heavy molecules sinking to the bottom, thus forming a stronger application than is intended; (2) that the acid causes extreme contraction of the arterioles through the vasomotor nerves; (3) that the difficulty arises from direct chemical action upon the vessels and tissues, accompanied by thrombosis; and (4) that an acute edema is produced, the tension of which, in the resisting tissues of the toes and fingers, is destructive to vitality. It does not seem unlikely that any one of these factors might at times be at fault, or even all of them combined, and that tight bandaging might also be occasionally concerned, although this has been strenuously denied by some investigators.

Treatment.—When gangrene is complete amputation is of course required, although a distinct line of demarcation should present itself before this is done. Valuable portions of fingers should not be hastily sacrificed, however; so that it may be better, in some instances, to allow the dead tissues to separate naturally from the living, and then nip off the bone high up with forceps, without doing a formal amputation. If only the skin has been lost, it may be possible to save the part by means of skin-grafting according to Thiersch or Krause.

As a matter of precaution, it is better never to employ solutions of carbolic acid under any circumstances where gangrene might supervene, especially as other and less dangerous antiseptics give equally good results. It should be noted that the cauterizing effect of carbolic acid is neutralized by the *immediate* application of strong alcohol. The hands, for instance, may be placed with impunity in pure carbolic, provided they be immersed at once in alcohol.

Ainhum is a peculiar disease of the little toe, although it may occasionally affect the other toes or rarely the fingers. It is almost exclusively confined to negroes, and is not infrequently met with in Africa and South America as well as other tropical and sub-tropical countries. A number of cases have been reported in the United States. The trouble manifests itself by the slow development of a furrow around the base of the toe, beginning on the under surface, as though a string had been tightly tied about the part, the epidermis within the groove becoming progressively thick and callous. The member is slowly strangulated by contraction of this epithelial band, and undergoes a species of necrobiosis ending in extensive degeneration of the tissues and accompanied by softening and absorption of the bones, especially of the terminal phalanx. Actual gangrene sometimes results, although rarely. Considerable swelling of the toe is usually present, often converting it into a ball-like tumor attached to the remainder of the foot by a small flexible pedicle. When the pedicle finally gives way, spontaneous amputation results. The process is very chronic, lasting from two to twenty years. It is practically painless except toward its termination, when ulceration of the adjacent portion of the foot may arise accompanied by considerable suffering.

The **cause** of ainhum is obscure. It has been variously attributed to nervous disturbances, arteriosclerosis, leprosy, traumatism, intentional ligation with strings, bacterial infection, etc. Unna regards it as "a species of circular scleroderma with the formation of epithelial callosities" and strangulation of the toe. Racial peculiarities and heredity play prominent parts.

The **treatment** is unsatisfactory and usually ends in amputation, although it is claimed that early division or excision of the constricting band may check the progress of the disease. (See Tropical Diseases.)

Microbic or Traumatic Spreading Gangrene, Emphysematous Gangrene, Gangrene Foudroyante, etc.—This is a virulent, rapidly spreading mortification due to infection with certain gas-forming microörganisms of several different species. Its nomenclature is confusing owing to the variety of names which have been applied to it, some of which are: *gaseous gangrene, molecular gangrene, traumatic emphysema, acute putrid infection, acute gangrenous septicemia, spreading traumatic gangrene, emphysematous gangrene, acute gangrenous edema, serous gangrenous infiltration, primary mephitic gangrene, progressive gangrenous emphysema, gas phlegmon, acute microbic gangrene, fulminating gangrene, gangrenous cellulitis, malignant edema,* and *anaërobic gangrene.* Clinically, anatomically, and histologically, however, there is probably but one type, although Kropác attempts to differentiate the existence of several distinct forms. It is characterized by rapid unlimited spreading, by the formation of quantities of gas within the tissues, and by intense toxemia. Formerly supposed to be due to the bacterium of malignant edema alone, we now know that it is caused by other germs as well, among which have been recognized the Bacillus aërogenes capsulatus (Welch and Flexner), the Bacillus proteus vulgaris, the Bacterium pseudo-œdematis maligni, and the Bacterium coli commune, the last named being most effective in the presence of diabetes. The Bacillus aërogenes capsulatus is probably the most frequent cause. It is commonly found in soil, in dust, and in feces. It is sometimes carried through the blood to distant regions, as in a case of gas-gangrene of the vulva observed by the writer, in which extensive secondary involvement of the subcutaneous tissues of the left shoulder occurred without lesion of the skin. Mixed infections also exist containing various forms of microörganisms which may or may not play a part in the process.

Symptoms.—As this form of gangrene is essentially an infection, it nearly always begins in a dirty wound, although it may arise secondarily through the blood. There is generally extensive injury of the tissues, for instance, a crush or a compound fracture, but the origin may be in a trivial abrasion or even so small a thing as the prick of a hypodermic needle. Dirty, contused, and lacerated wounds such as are received in street and railroad accidents are more liable than others to this sort of infection, particularly if the bones are likewise crushed. It occurs in the region of the genitalia with relative frequency.

In most other forms of mortification the limb dies first and infection takes place secondarily; but in the foudroyante variety infection occurs primarily and gives rise to the gangrene as its direct sequence. Hence the first evidence of trouble is in the immediate vicinity of the wound, where the characteristic changes may appear within eight to twenty-four hours after an injury, or even sooner, especially if the parts have been kept warm and moist. The spread of the disease is often astonishingly rapid, with no tendency to the formation of a line of demarcation—an entire extremity sometimes being involved from one day to the next. The skin is usually at first dusky-red, although it may remain almost normal in color for some time after emphysema has appeared. It soon turns brownish and then black, often with a strong tinge of green, and it may be marbled by thrombosed veins. The epidermis is frequently raised in blisters containing foul fluid dark with blood-pigment. The progress is often irregular, extending finger-like up one side of a limb more rapidly than the other. Red lines, representing lymphangitis, lead to the nearest lymph nodes, which rapidly enlarge. The extremity becomes swollen and tense, and the tissues fill with gas, so that crepitation is easily elicited on pressure. If an incision is made through the skin a dark, watery, offensive, bloody fluid mixed with gas will bubble out of the opening, and gangrenous connective tissue can be seen beneath. The muscles are involved early and become disintegrated and pulpy. If the patient live long enough the original wound is found to be filled with dark flabby sloughs.

In typical cases there are no indications of inflammatory reaction and of course no pus; but in mixed infections both inflammation and suppuration may be present if death does not come too quickly. Instead of a form of inflammation, this rapidly spreading gangrene must be regarded as a pure fermentation, which view is supported by the fact that it will take place in dead tissue as well as in the living (Hitschmann and Lindenthal), The gases which permeate the tissues are said to be formed by the action of microörganisms upon the glycogen of the muscles, the connective tissue having little to do with the process actively.

An autopsy reveals no changes in internal organs except cloudy swelling; unless the bacilli have invaded the blood-vessels after death, when the viscera may be filled with gas, thus giving rise to so-called "foamy organs."

The general symptoms, although they are occasionally remarkably mild, are usually those of profound sepsis. There is a weak and rapid pulse, subnormal temperature, feeble capillary circulation, anxious expression, involuntary evacuations, and often a cloudy intellect or even unconsciousness. The prognosis is bad, although cases sometimes recover with operation or even without it. Out of 61 cases collected by Stewart, 55 per cent. died. Where gas develops slowly recovery is more likely.

The most effective **treatment** is early amputation through apparently sound tissues, when the gangrene is in a situation where this can be done, and even then failure often results. It has been advised to brush the flaps with pure carbolic acid, but there is nothing to be gained by this if the operation has been done aseptically and in non-infected tissues, and it can be of no use if the parts are already infected. In cases which have not progressed too far, especially if the origin is in a small injury or upon the trunk, Doerfler advises multiple free incisions followed by copious antiseptic irrigations and moist dressings. There can be no doubt that such treatment is sometimes followed by success, possibly due to the admission of oxygen to the anaërobic microbes; but most authorities agree that it is far less certain than early amputation. Incisions must, of course, be depended upon in situations where an amputation cannot be done. They must be numerous, deep and free enough to admit air to the diseased tissues—even into the muscles themselves. It has been suggested that irrigation with hydrogen peroxid or potassium permanganate might be of advantage, on account of the anaërobic character of the infecting bacteria. It is, of course, understood that the patient must be well stimulated and sustained by food. Water should be given freely by the mouth, and normal salt solution by the bowel and possibly subcutaneously. Intravenous injections are sometimes helpful.

Gangrenous cellulitis is a variety of traumatic, spreading, microbic gangrene, differing from the ordinary form in no way except that its most striking manifestations appear in the subcutaneous cellular tissues, which become rapidly distended with offensive dark fluid mixed with gas. It is caused by the same microörganisms acting in the same way. Crepitation is readily felt on manipulation of the discolored skin, and in bad cases the process extends rapidly with general symptoms of the gravest sepsis. Comparatively mild forms, however, are not infrequent, especially in the abdominal wall following the opening of virulent appendical abscesses. Here the colon bacillus is probably the most common cause. Multiple incisions with thorough drainage, moist dressings, and frequent antiseptic irrigations are usually effective in checking the process; although considerable loss of aponeurotic and fascial tissue may ensue, leading to postoperative hernia.

That spreading microbic gangrene may be due to other than gas-forming microörganisms is undoubtedly true, although it is comparatively seldom encountered and does not belong to a definite type. It is sometimes seen in erysipelas or following an injury and is usually due to the Streptococcus pyogenes. A low resisting power of the tissues is often present, produced by diabetes, chronic nephritis, debilitating fever, injury, etc., or the nutrition of the part has been seriously interfered with by circulatory disturbances from thrombosis or traumatism, as in injury to the popliteal artery followed by hemorrhage beneath the deep fascia and arrest of collateral circulation by pressure of the clot. Mortification produced by the cause last mentioned may not stop at the border of the ischemic area, but pass rapidly beyond it into tissues whose blood-supply is undiminished; this tendency to spread being dependent upon the presence of bacteria, which are usually gas-forming but may be of other species, for instance, those of ordinary infection, and putrefaction. The treatment of such microbic spreading gangrene must be equally prompt and energetic with that of gas-gangrene, immediate amputation being indicated when practicable, although multiple free incisions followed by copious antiseptic irrigations are sometimes effective. When arising from injury of an artery in an extremity amputation above the ischemic area must be promptly resorted to in order to prevent unlimited spreading. (See chapter on Diseases and Injuries of Blood-vessels.)

Hospital Gangrene (also known as *contagious* or *pulpy gangrene, sloughing* or *gangrenous phagedena, wound diphtheria, putrid degeneration, malignant sloughing, putrid ulcer, camp gangrene,* etc.).—Before the days of surgical cleanliness and the intelligent regulation of hospitals, gangrene was extremely common, especially in overcrowded field-hospitals and troop-ships in times of war. It often arose in epidemics which fairly decimated the wards of an institution, few patients with wounds escaping its frightful ravages. Infection from one individual to another, combined with unhealthy surroundings and overcrowding, were the prime causative factors.

In the writings of older authorities all kinds of microbic mortification were comprised under hospital gangrene; but in the course of time the term became more accurately applied to a certain definite variety, which is well defined by Erichsen as "a disease characterized by a rapidly destructive and spreading ulcer, covering itself as it extends by an adherent slough, and attacking open sores and wounds." Under our modern ideas of the treatment of wounds and the management of hospitals the disease has practically disappeared, probably never to return.

Erichsen further says: "When sloughing phagedena invades a wound that is previously perfectly healthy, the surface of the sore becomes covered with gray, soft points of slough which rapidly extend until the whole of the ulcer is affected. At the same time it increases rapidly in superficial extent, and commonly in depth, the surrounding integument becomes edematous, swollen, and of a livid-red color; the edges of the ulcer are everted, sharp-cut, and assume a circular outline, and its surface is covered with a thick, pulpy, grayish-green, tenacious mass, which is so firmly adherent to the sore that it cannot be wiped off from it, being merely swayed to and fro when an attempt is made to clean it. There is usually some dirty yellowish-green or brownish discharge, and occasionally some bleeding; the pain is of a severe burning, stinging, and lancinating character, and the fetor from the surface is considerable. The ravages of the disease when fully developed are very extensive. The soft parts, such as the muscles, cellular tissue, and vessels, are transformed into a gray, pulpy mass and the bones are denuded and necrosed." The constitutional symptoms are those of septic intoxication.

Whether the cause of this frightful malady is a specific microörganism or not is now difficult to determine; but it is more likely that various germs, including those of suppuration, are concerned in its production, aided by a low resisting power of the tissues, from unhygienic surroundings, sickness, debility, etc.

The prophylactic **treatment** consists in surgical cleanliness, combined with good hygiene and avoidance of overcrowding. The disease itself is best arrested by the thorough application, usually under general anesthesia, of pure nitric acid, acid nitrate of mercury (Keen), bromin, chlorid of zinc, the actual cautery, etc., followed by moist antiseptic dressings. Prior to cauterization it is well to remove the sloughs with forceps and scissors, avoiding injury of sound tissues. Stimulants and nourishment must be freely administered.

Sloughing Gangrene is simply a species of rapidly progressive ulceration in which the sloughs are sufficiently large to deserve the designation of gangrenous masses. Between this and **phagedenic gangrene** there is no real difference. Both terms were formerly used as synonyms of hospital gangrene, but at present they are rather infrequently employed to designate much less virulent although sufficiently serious processes which are sometimes met with, particularly in bedsores and certain venereal ulcerations in debilitated individuals. They are caused by the action of ordinary infective microörganisms on tissues of low resistance.

In treating such conditions attention must always be given to food, stimulation, and general hygiene. Locally, a thorough cauterization of the ulcer is usually indicated, with strong nitric or carbolic acid or the hot iron. Often enough, however, removal of the sloughs with scissors, and the application of a wet antiseptic dressing, will be sufficient.

Noma, Cancrum Oris, or Gangrenous Stomatitis is a rare form of microbic gangrene, occurring almost exclusively in children under ten years of age, and always following some debilitating sickness. It is so uncommon that but 6 cases occurred among 13,000 patients admitted to the Hospital for Sick Children in London. It usually involves the mouth and cheek, although occasionally attacking the vulva, the anus, the umbilicus, or even the skin of the extremities. The disease now seldom appears in adults in this country or in Europe, although it is said to do so with frequency in India. For some unknown reason, girls seem much more susceptible than boys. Most cases are sporadic, but epidemics of considerable severity have been observed from time to time, which argues with probability the communicability of the disease from one patient to another.

Causes.—Perhaps one-half the cases follow measles, typhoid coming second as a predisposing cause. It has also been met with after scarlatina, whooping-cough, variola, diphtheria, dysentery, bronchopneumonia, cholera, etc. It does not seem to be the specific disease which causes the difficulty, so much as the consequent debility and lowering of tissue-resistance. That bad hygienic surroundings and lack of care are factors of importance cannot be denied; but that noma may arise under the most favorable conditions has been abundantly proved by observation.

The gangrene is undoubtedly due primarily to microörganisms and not to vascular changes or nervous influences; but a specific microbe has not yet been isolated with certainty, and it is quite possible that one does not exist, although many observers have made more or less decided claims in this regard. The difficulties attending bacteriologic investigations in a gangrenous process about the mouth can easily be appreciated, as the sloughs are apt to be filled with every sort of germ that inhabits the buccal cavity. Numerous varieties of bacilli and cocci have been found, and especial attention has been called to a species of leptothrix by Blumer and MacFarlane, Perthes and others, which is probably the same germ as the "spirochete of necrosis" (Herman). Matzenauer has endeavored to prove that noma is identical with the "hospital gangrene" once so prevalent in institutions for the sick; and it is quite possible that he may be correct, as the appearances and symptoms of the diseases are very similar.

Symptoms.—Noma nearly always begins within the mouth, upon the mucous membrane of the cheeks or possibly the gums, although occasionally it is first observed externally. In most instances the point of origin is apparently a simple ulcer, but sometimes an infiltration of the mucosa and subjacent tissues seems to precede its full development. Rapidly spreading gangrene soon makes its appearance, nearly always of the moist variety, but sometimes dry. The tissues become dusky-red, purple, and then black, the borders of the necrotic area being indurated from infiltration, and reddish-brown in color. The appearance of a dark spot upon the skin externally is soon followed by gangrene and perforation of the cheek, the soft parts being transformed into grayish-black, pulpy sloughs. From the mouth and through the hole in the cheek flows a horribly foul acrid discharge.

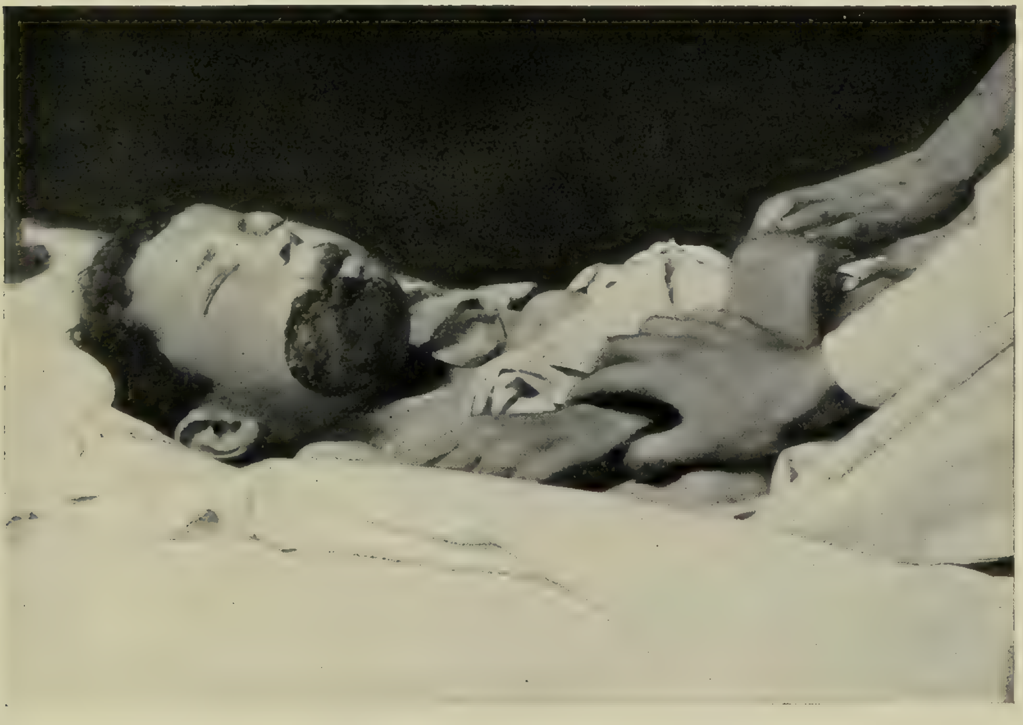


FIG. 80.—NOMA AFTER TYPHOID FEVER (Sailer).

The disease may confine itself to the buccal mucous membrane, although it rarely does so, and may become arrested at any time; but usually a considerable hole is eaten out of the cheek, and loss of the lips, nose, eyelids, and even portions of the forehead can occur, with implication of the maxillary bones. In the genital region the entire vulva may become gangrenous with destruction even of the recto-vaginal septum. The disease is subject to remissions and exacerbations, the former often leading to false hopes of speedy recovery which are seldom realized.

The *general symptoms* are usually those of overwhelming sepsis, although strangely enough in some of the most disastrous cases this is not true. The mind becomes cloudy, as in typhoid, the pulse feeble, and the temperature, which is at first high, may fall later to normal or below it as poisoning increases. Disturbances of the digestive tract and inhalation-pneumonia are apt to result from the putrid discharges.

The prognosis is bad, about 75 per cent. of the cases being fatal within ten days or two weeks. This is hardly to be regretted when we consider the horrible and hopeless deformities of the face resulting from loss of tissue, which often require plastic operations taxing to the utmost the resources of the surgeon.

Treatment.—The mouth of every child suffering from a severe debilitating illness, especially measles, should be kept scrupulously clean and carefully watched. Carious teeth should be attended to. If an ulcer is detected, no matter how harmless it may seem, it should be cauterized with nitrate of silver or pure carbolic acid.

When gangrene is established there is but one effective treatment, which consists in burning out the infected area with the actual cautery. This should be thoroughly and fearlessly done, until sound tissues are reached, because the damage done by a hot iron will be small compared with the possible ravages of the disease. Runke prefers, however, to extirpate the disease with a knife, while others advise simple curettement followed by chemical cauterization and antiseptic applications; but these methods are not in general use except under special conditions or in mild infections.

Ludwig's Angina; Angina Ludovici or Ludwigii.—This is an acute inflammation of the lymph nodes and connective tissue within the capsule of the submaxillary salivary gland. It is always serious in character, and sometimes results in gangrene involving the intracapsular tissues, or even the floor of the mouth or the structures of the neck, such serious consequences coming from the extreme tension to which the inflammatory products are subjected. It is frequently confused with more superficial suppurations of a much less dangerous character.

The trouble begins in the lymph nodes, infection being derived from the teeth, tonsils, or ulcerations within the mouth. The salivary gland is not concerned in the process, except secondarily. The most frequent cause is the Streptococcus pyogenes, although sometimes the staphylococcus is found, and occasionally other germs, such as the colon bacillus.

Symptoms.—Chills and high fever characterize the inception of the disease, followed soon by difficulty in swallowing and breathing. A hard, sensitive, deep-seated swelling appears in the submaxillary region, which cannot be definitely outlined as in more superficial glandular involvement. Unlike an ordinary phlegmon, redness of the skin does not manifest itself at first, but after several days only, when the inflammation has become extra-capsular. Marked tumefaction of the floor of the mouth takes place, forcing the tongue upward against the palate, and edema of the glottis may result, leading to symptoms of suffocation. There is more or less ankylosis of the jaws, and the partially open mouth overflows with saliva of a foul odor. Septic intoxication is profound, the patient often dying from this or from edema of the glottis. The mortality is as high as 50 per cent. if operation is not promptly resorted to.

The only effective **treatment** is an early and free external opening of the submaxillary capsule, timid and superficial incisions being ineffective. If the onset is severe and the poisoning great, an operation should be done even before the formation of pus, and without waiting for fluctuation, which seldom appears at any time. Owing to the proximity of important nerves and vessels, it is better, after division of the skin, to burrow through the subjacent tissues into the glandular capsule with some blunt instrument, such as a pair of hemostatic forceps. In case of impending suffocation an immediate tracheotomy may be necessary in order to save the patient's life. Intubation is well-nigh impossible owing to tumefaction of the tongue and floor of the mouth. (See Surgery of the Neck.)

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CHAPTER IX.

PROCESS OF REPAIR.

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I. Historical Introduction.

A knowledge of the processes by which repair takes place in wounds has long been recognized as of great importance, not only from a purely theoretic point of view but also from a practical aspect, as determining the factors which aid or impede the course of healing, thus placing the surgical treatment of injuries on a firm scientific basis. Records of studies on this subject date back many centuries and are found chiefly among the archives of the warlike nations, of whom the Greeks especially have recorded many interesting observations on wounds and repair. Indeed, we owe to Hippocrates (400 B. C.) the classification of wounds still employed.

Hippocrates divided wounds into those made by a sharp weapon and healing primarily, or without suppuration, and those due to blows with blunt instruments where the tissues are crushed and healing is accomplished only after suppuration and the formation of granulation tissue, in other words, by secondary union. A somewhat crude and empiric antiseptic treatment of clean wounds is recommended in his writings, including directions for boiling the water used in washing the incision and calling attention to the proper cleansing of the hands.

In the treatment of crushed wounds the promotion of early suppuration is recommended, a mode of treatment which has continued until quite recent times and still shows its early influence on the theory of healing in the term "laudable pus," not quite obsolete among some of the surgeons of the older school. Rest and immobilization are recognized by Hippocrates as most important factors in promoting healing.

Celsus (50 A. D.) added but little to the lore of wound healing as given by his great predecessor in medicine five hundred years before, confining his writings chiefly to the therapeutic aspects of the subject; but the books of Galen (200 A. D.) give many details concerning repair after injury, although they are not strikingly original but are based largely on the teachings of the Hippocratic school. Galen employed the Hippocratic classification of primary and secondary union in wounds, subdividing each group, however, into those with and those without loss of substance. Even in clean wounds with loss of substance, repair must take place by the formation of granulation tissue, which he considered as derived from the blood, the final result being the formation of a cicatrix. He distinguished two forms of wound secretion, one fluid, or pus, the other solid, or scab.

The teachings of these three great masters in medicine were preserved for many centuries by a group of pupils of the Alexandrian school, though without any additional light being thrown on the subject.

With the extinction of the Græco-Roman civilization, the task of preserving the wisdom so far gained fell chiefly on Arabian physicians, who, however, neglected the advice of Hippocrates to base knowledge upon experience, and contented themselves with editing Galen. They did not, therefore, contribute in any noteworthy degree to advance our knowledge of repair. In fact, the lack of technical facilities and of anatomic knowledge rendered it impossible at that time to proceed much further in the study of repair by mere clinical observation, so that it was not until the discovery of the circulation of the blood by Harvey (1619), and especially of the flow in the capillaries by Malpighi (1661), and until the improvements in the microscope permitted a more thorough study of the tissues, that our knowledge of wound healing increased. Perhaps the greatest name in this connection is that of John Hunter (1770), one of the first great experimental pathologists. His observations, though influenced by those of his immediate predecessors and the necessarily imperfect technic of the times, were characterized by such originality and sound judgment that they have served as models for much of the experimental study of wound healing since his time.

Wounds, according to Hunter, were closed in three ways: (1) Primary or immediate union. (2) Healing by inflammation, a process which incited a flow of "coagulable lymph" (fibrin, cells, and serum), the lymph cementing the apposed edges of the wound. After the absorption of the red corpuscles, nerves and vessels were formed in the lymph which remained. (3) Secondary union or healing by granulation. The granulations were formed from the coagulable lymph and in open wounds were usually preceded by suppuration, which is a preparative process. He noted that in subcutaneous injuries, however, granulation tissue may be formed without the intervention of a suppurative process.

Hunter included healing under a scab in a separate heading because it bore resemblances both to healing by primary union, from the moderate amount of inflammatory reaction, and to suppurative inflammation because of the occasional formation of pus and granulation tissue under the crust.

While the conservative nature of the granulating process was generally recognized, Hunter insisted that pus should not be regarded as a corrosive fluid resulting from the breaking down of solid tissues, as had been suggested by Hippocrates, but rather as a healing fluid which prepared the way for healthy granulations. He considered pus as a secretion from the vessels, though not present as such in the blood.

Astley Cooper (1825) also lays stress upon the essentially conservative nature of inflammation and states that even the smallest wounds would prove serious without the healing influence of the inflammatory process.

Paget (1853) distinguished five modes of wound healing: (1) By immediate union; (2) by primary adhesion; (3) by granulation; (4) by secondary adhesion or the union of granulations, also called union by third intention; (5) by healing under a scab.

He failed to observe that there are only quantitative differences between the so-called immediate union and union by primary adhesion, both forms really corresponding to what we now term primary union. The only difference between the two is in the amount of exudate poured out between the apposing surfaces. Paget still followed Hunter in considering that the exudate of coagulable lymph organized into fibrous tissue, but demonstrated that the blood-clots in a wound do not aid healing but rather interfere with it and must first be got rid of before healing takes place.

The discovery of nuclear division in cells led Virchow (1855) to apply the new facts to pathology and to derive the cells in the healing wound only from cells already present in the wounded tissues under the influence of a "formative stimulus." The organization of the "plastic lymph" of Hunter or the formation of "blastem," upon which so much stress was laid by Paget, was, according to Virchow, only the result of growth of connective-tissue cells, while pus cells were formed *in situ* as derivatives of epithelium, connective tissue, or possibly of muscle and nerve cells. The relation of the vessels and the blood to the healing process was, according to this view, relatively unimportant. As usual, the theory was carried to an extreme, and on the authority of Virchow the old Hippocratic view, that pus results from the breaking down of tissue, was thus again resurrected, despite the vigorous objections which Hunter had raised eighty years before.

A second step toward the modern view of inflammation and repair we owe to Cohnheim (1867), who in a classic paper showed that the formation of an exudate containing pus cells was due to an alteration in the walls of the blood-vessels which permitted plasma, leukocytes, and red corpuscles to pass out into the tissues. He still held, however, to the old view that these emigrated leukocytes were capable of forming fibroblasts or connective-tissue cells. The factors in the healing process, according to Cohnheim, consisted of a combination of regeneration and inflammation, the regeneration chiefly taking place in the epithelial tissues, while the loss of the subcutaneous tissue was replaced by an inflammatory growth of connective-tissue cells and leukocytes.

We now come to the last phase of the knowledge of wound healing as developed in the past twenty years, chiefly through the efforts of the German school of pathologists, though important contributions have been made by various French observers. The different aspects of the subject as unfolded during this period can perhaps be most conveniently viewed in connection with the study of the relations between inflammation and repair in the sections which follow, even though some repetition may be necessary.

The trend of the studies on repair which have occupied this period has been partly toward attempting a final decision as to the relative importance of the various phenomena already known as taking part in the process of repair, and partly toward the proper evaluation of the newer conceptions, such, for example, as the theory of "slumbering cells" (Grawitz), of phagocytosis (Metchnikoff), the various activities which bacteria or their products exert upon the tissues, the part played in inflammation and repair by bactericidal substances, antitoxins, or other antibodies, the rôle of cellular and autolytic ferments, and, finally, the nature of that formative stimulus which incites the overgrowth of cells. In the attempt to solve the fundamental problems of inflammation and repair, the lines of investigation have broadened and of late years comparative pathology has accomplished much that is suggestive in this regard. Metchnikoff studied phagocytosis from the standpoint of a zoölogist, and investigated the defensive and reparative processes seen in the lowest types of animal life. Loeb, who has opened a new path for the study of the action of various stimuli, whether formative or inhibitory, under conditions which can be expressed in terms of physical chemistry, employed the egg cells of the star-fish, sea-urchin, and other of the lower forms of sea life. Experimental data from these simple types of beings are more easily obtainable and the conditions are more conveniently controlled than in mammals, but the results so obtained are not directly transferable to the human subject. They offer, rather, suggestions for further studies so necessary for the complete understanding of the complicated process of repair, for, as will be seen later, while we have at present a fairly consistent knowledge of the major phenomena connected with healing, there is still much to learn as to the details and finer relationships between the various elements involved.

II. GENERAL CONSIDERATIONS.

DEFINITION OF REPAIR.

The result of the processes by which injured tissues are restored to a condition more or less approximating the normal is known as repair or healing.

Repair in a surgical sense is usually considered in connection with wounds, using the word wound to denote a recent solution of continuity in the tissues. Such an injury may be due to external violence produced by any hard body or by a fall causing a tear in one of the internal organs.

Wounds produced by external violence may be sharply defined and limited to the skin and subcutaneous tissues—simple wounds; or they may be rendered complex by connection with other conditions, such as, for example, a fracture of an underlying bone, injury to a solid or hollow viscus, or the penetration of one of the body cavities—complicated wounds.

Both varieties of wounds may be produced by sharp or blunt instruments or by fragments of shells or projectiles. Wounds due to projectiles are usually classed from a clinical point of view as gunshot wounds, but the nature of the reparative process is the same as in injuries due to other agents.

The term wound is not, however, necessarily confined to the injuries of soft tissues, for it is quite proper to speak of a wound of bone, as in an injury to the cranial bones produced by a cutting instrument, or when a long bone has been perforated by a bullet.

In considering the general subject of repair it is proper to include some forms of tissue injury other than wounds due to physical or chemical agents, an example being the healing of burns produced by heat or of the necroses due to the action of the X-rays or of radium.

These differences in the methods of production or in the nature of wounds influence healing chiefly from a quantitative point of view. The repair is achieved largely by the proliferation of the same tissues in all cases, but the amount of the scar tissue formed, the time required in healing, etc., vary in different types of wounds.

CONTRAST AND RELATION BETWEEN REPAIR AND INFLAMMATION.

For the intelligent comprehension of the nature of the reparative processes which lead to healing after various types of injury, it will be necessary to consider briefly certain phases of the closely related conditions which accompany the purely reparative phenomena and are collectively designated as inflammation.

As has been previously pointed out, the clinical phenomena which accompany inflammation have long been known. The reddening of the inflamed tissues, the heat which can be noted by the hand, the swelling, and the pain are still as important clinical symptoms of inflammation as they were in the days of Celsus. In recent times another symptom, loss of function, has been added.

The ancients recognized the fact that wounds which did not exhibit heat, redness, or swelling healed more promptly than those which did, and their efforts were directed to the prevention of such conditions or to their removal if present. The unpleasant results which followed the manipulation of fresh wounds by unclean hands or instruments formed a portion of the surgical knowledge of the early Greeks, and they tried to avoid the infection of clean wounds by the use of what we would now designate antiseptic fluids. Inflammation was to them, therefore, a harmful process which interfered with healing.

The physicians of the middle ages, having noted that general sepsis was less frequent after free suppuration had induced the formation of granulation tissue, lost sight of the possibility of obtaining primary union, and infected fresh wounds in order to obtain early inflammation. To them inflammation was a thing impossible to avoid and, in one of its phases, conservative in nature. This attitude persisted until Pasteur and Lister showed that suppuration could be avoided by cleanliness and antiseptics; yet the theory was not without some foundation, for we now know that granulation tissue does not permit the passage of bacteria through it into the deeper tissues and thus prevents the entrance of pathogenic germs through the wound surface.

Though some of the older surgeons inclined to the belief that inflammation was a necessary preliminary to healing, and therefore in its last analysis a conservative process, it remained for Virchow to lay the foundation of the modern views concerning its nature. He regarded inflammation as a local alteration of nutrition determined by external agents acting on the affected area and inducing cell growth by the action of formative stimuli. He called attention to the anatomic changes underlying the clinical evidences of inflammation, such as the vascular dilatation and increased circulation as a cause of the redness and heat, the dependence of the swelling upon the presence of an exudate, the pain as an evidence of irritation of the nerves of the part, etc. The discovery of the emigration of the blood-corpuscles from the vessels directed attention to the relation of the cells to the exudate and away from the changes in the cells of the inflamed tissues. According to this view, the healing of wounds is due to regeneration and productive inflammation, the cells forming the granulation tissue being derived from the blood. It is interesting to note in passing the reversion to the views of Galen as previously given.

Weigert (1886) in turn again emphasized the important rôle of the tissue cells, and, reversing the theory of Virchow, stated that the multiplication of cells observed during inflammation cannot be considered as an active process due to a vital stimulus, but that the destruction of the tissue cells induced by the irritant gives free scope to the natural and vital regenerative powers of the remaining healthy cells, usually at some distance from the injury. The proliferation of these cells was therefore purely regenerative and not due to the inflammation.

The discovery of the rôle of bacteria as inciting agents in inflammation is perhaps of greater importance from a practical standpoint in wound treatment than as assisting in unraveling the nature and relations of inflammation and healing. The study of the action of the various microorganisms on the tissues has led to a great increase in our knowledge of the selective action of the toxins which they produce on the various body-cells. We see, for example, that the Staphylococcus pyogenes exerts a marked chemotaxis on the polynuclear leukocytes, the toxin of the gonococcus attracts the eosinophile group, the tetanus toxin acts chiefly upon the nervous system, the products of the tubercle bacillus incite the formation of characteristic lesions, and so on. But, after all, the bacterial products merely incite reactive phenomena in the body-cells, just as may any other chemical substance. Many of the same anatomic changes may be produced in the absence of bacteria. The fundamental nature of the process is the same.

Others have adopted a more or less modified form of Weigert's hypothesis, among whom may be mentioned Marchand and Ribbert. Leber was among the most earnest defenders of the position that inflammation is, on the whole, a conservative and reparative process, a view with which Marchand fully agrees. A very full and clear exposition by Adami of the subject from the same position has recently appeared.

On the other hand, we must not forget that the practical surgeon is not apt to recognize a conservative agent in the various phases of an acute or chronic inflammatory process, and perhaps regards the exudate or profuse purulent discharge coming from an infected wound as an evidence of destruction rather than of repair, and the contraction of a cicatrix following extensive granulation as a far from useful phenomenon. He is therefore likely to consider inflammation as a result of infection and to separate it more or less arbitrarily from the reparative process. The phenomena which may be observed after an aseptic injury are frequently designated "aseptic inflammation" or "aseptic fever," and the clinician is apt to suggest that the changes which take place are an expression, not of inflammation, but of repair, although he cannot deny that the anatomic changes produced by a subcutaneous trauma, as, for example, a sprain or fracture, are microscopically the same as those seen in an infected wound, although bacteria are not concerned in the process. These tissue changes, then, are regarded as "reparative" if no bacteria are present. If, however, bacteria invade the tissues, the formation of an exudate, the necroses and degeneration caused by the trauma and the toxic products of the bacteria, produce a condition which he calls inflammation, though it may be qualified by the use of the term "infective inflammation" to distinguish it from "aseptic inflammation." In other words, a distinction is made between the reparative processes which take place under aseptic conditions and those occurring in inflammation or septic conditions, and the term inflammation is reserved to designate the "series of results caused by microbic interference with the normal process in repair in injured, living tissues" (Nancrede). These inflammatory changes, according to this point of view, usually lead for a time to the destruction of tissue, but are ultimately conservative in their nature, the final results being the removal or neutralization of the microbic causes. Under these assumptions, therefore, there can be no aseptic inflammation, that process not being inflammatory in nature but wholly reparative; and the only terms necessary are repair and inflammation; the latter under ordinary conditions always denoting a process due to the action of germs or their products. The tissue changes seen during normal repair should therefore not be termed inflammation, though it must be acknowledged that at certain stages the reparative process and the inflammatory process result in similar morphologic appearances. According to this classification, the production of a sterile exudate by the subcutaneous injection of irritating substances, such as turpentine, etc., need not be considered as anything but an artificial condition.

Despite this arbitrary disposal of the matter the clinical use of injections of the salts of mercury in the treatment of syphilis not infrequently leads to the formation of reddened, indurated areas, commonly designated as inflamed; and occasionally the tissues injured by the toxic salt break down and discharge a fluid which, though sterile, is ordinarily designated as pus: an illustration of some of the difficulties of obtaining a complete classification and a consistent nomenclature of the phases of a phenomenon so complex as that of healing.

From the preceding discussion it will be seen that the most generally accepted view of the phenomena which we are accustomed to designate by the term inflammation is that they represent not only a local but also a general reaction of the cells of the body to an external injury.

The force which produces an injury may be either physical or chemical, and its application results in the induction of corresponding changes in the tissues. The chemical irritants are the most important practically and are commonly produced by the growth of bacteria, certain species of which have the power of forming substances which act injuriously upon the cells of the tissues.

The injury to the tissues produces cell degeneration and renders more active certain physiologic powers of the body-cells in virtue of which they proliferate more actively than is normal, permit the formation of an exudate, give off ferments and anti-bodies, or act as phagocytes.

The trend of the new growth of cells thus incited is adaptive in its nature and leads to a production of new tissue which tends more or less perfectly to repair the injury which has been produced.

GENERAL METHODS OF REPAIR.

Repair in Nonvascular Tissues.—Any injury which calls for the exercise of the reparative powers of the tissues incites collateral changes in the neighborhood of the wounded area which are commonly included under the general term inflammation. The simplest example of such action is seen after infliction of an uninfected incision into the cornea. A few epithelial and connective-tissue cells are destroyed by a purely traumatic action. Before healing can take place the dead cells must be removed either by phagocytes or by solution of the dead tissue under the influence of ferments derived possibly from the injured cells themselves (autolysis). The ferments or the toxic products of cell destruction thus set free act upon the surrounding tissues and attract wandering cells from the neighboring conjunctival vessels or sac to the injured area (chemotaxis). At the same time there occurs an outpouring from the tissue spaces of fluids, which under the influence of the cell juices form a small amount of fibrin (exudation). The connective-tissue cells of the cornea and the epithelial cells covering it soon begin to proliferate (regeneration), and ultimately fill up the gap in the tissues (healing). The trauma produced by the knife has destroyed cells and thus incited regeneration. If instead of mechanical injury the cornea had been etched with a stick of silver nitrate or burned with a hot needle, the phenomena induced would have been more extensive, but the healing would have been accomplished by the same successive steps.

All of the clinical features of inflammation are missing in the first case, except pain and swelling. If the cauterization or burning is repeated, vascularization of the cornea from the sclera and conjunctiva may take place with the formation of granulation tissue and the exudation of numerous leukocytes to form pus. Redness is present if the vessels are numerous and function is interfered with by the keratitis which results in an opaque scar due to the lack of transparency of the fibrous tissue cicatrix.

The same phenomena will be observed if such a simple wound is infected with a culture of Staphylococcus pyogenes; the toxins of the bacteria incite more necrosis of the tissue and produce an exceedingly active chemotaxis, the cornea is vascularized, with the end result of a large opaque area due to the destruction of the true corneal tissue and its replacement by scar tissue. In this type of inflammation the other clinical symptoms appear which were missing from the clean wound, *i. e.*, redness and heat.

Repair in Vascular Tissues.—The initial stages of inflammation and repair in vascular tissues are so closely related to changes in the circulation that it is necessary to observe them in thin membranes such as the mesentery of a warm-blooded animal where the capillaries can be directly observed under the microscope. The change first noted under these conditions is a dilatation of the vessels which is most marked in the arteries and is accompanied by an increased rapidity of the blood-stream. In a short time after the exposure of the delicate membrane to the desiccating action of the air, the blood-current in the vessels becomes slower, and if a small vein or capillary is carefully examined it will be noted that the white corpuscles have a tendency to occupy a position close to the wall of the capillary or roll along it, while the red cells still flow in a compact, axial stream. The current gradually becomes slower until finally complete stasis may occur. Occasionally the stream again resumes its course, leaving the inner surface of the capillary plastered with adherent leukocytes. If attention is now directed to the endothelial wall of the vessel it will be noted that the leukocytes begin to pass through that membrane at a point where two cells join. The blood-cell appears on the outside of the vessel as a bright spot, and gradually the entire body of the leukocyte follows the first projection. In the course of six or eight hours a large number of leukocytes have emigrated and a few red cells, together with some plasma, have been carried into the tissues. The formation of fibrin can be noted in the tissue spaces if the exudate is allowed to remain for a considerable time. This is the first stage of inflammation, definite reparative procedures not having as yet begun. If such inflamed tissue is returned to the peritoneal cavity, bacterial infection having been avoided, repair may take place by the return of the circulation, the removal of the leukocytes and red cells through either the lymphatics or the blood-vessels, or by their destruction and absorption by phagocytic cells derived from the peritoneal surface.

If a small vessel is compressed the formation of a thrombus in the lumen can be observed, this thrombus being formed of blood-platelets. If the lumen is permanantly occluded the platelets collect and form plugs on either side of the point at which the vessel is closed. Red and white cells and fibrin are also deposited in the small thrombi. If the mesentery is injured so that the capillaries are torn across, the formation of a blood-clot which closes the wound and cements the opening of the vessel may also be followed.

Regenerative changes in the surface epithelium of the mesentery do not begin until some six or eight hours after the injury of the tissue, so that it is difficult to follow their growth in the exposed membrane. The tissues, however, can be fixed and then examined after appropriate staining. It will be found that the peritoneal epithelium begins to cover a wounded surface by virtue of its ameboid capacity and thus to repair the damage produced by the trauma.

A further stage of healing in aseptic wounds can be studied in sections made from the skin of animals where a reparative hyperplasia of the connective tissue begins to be evident after twelve to twenty-four hours, as shown by the swelling of the cell-bodies and the thickening of the nuclear chromatin with the formation of occasional mitotic figures. These changes increase for forty-eight to seventy-two hours after the wound had been made, and form the granulation tissue which results in definitive healing. Careful studies of the granulation tissue will show phases of the process which were observed in the mesentery of the live animal but which have been arrested by the fixative reagent. Leukocytes can be seen distorted into long cylindric forms as they pass from the lumen to the adventitial cells about the newly formed blood-vessels (Fig. 88). The fibrin network and the exuded red cells can also be seen. The surface epithelium of the skin proliferates in response to the injury and covers the surface of the granulation tissue. The further details of the healing by granulation tissue are considered in the section treating of secondary union.

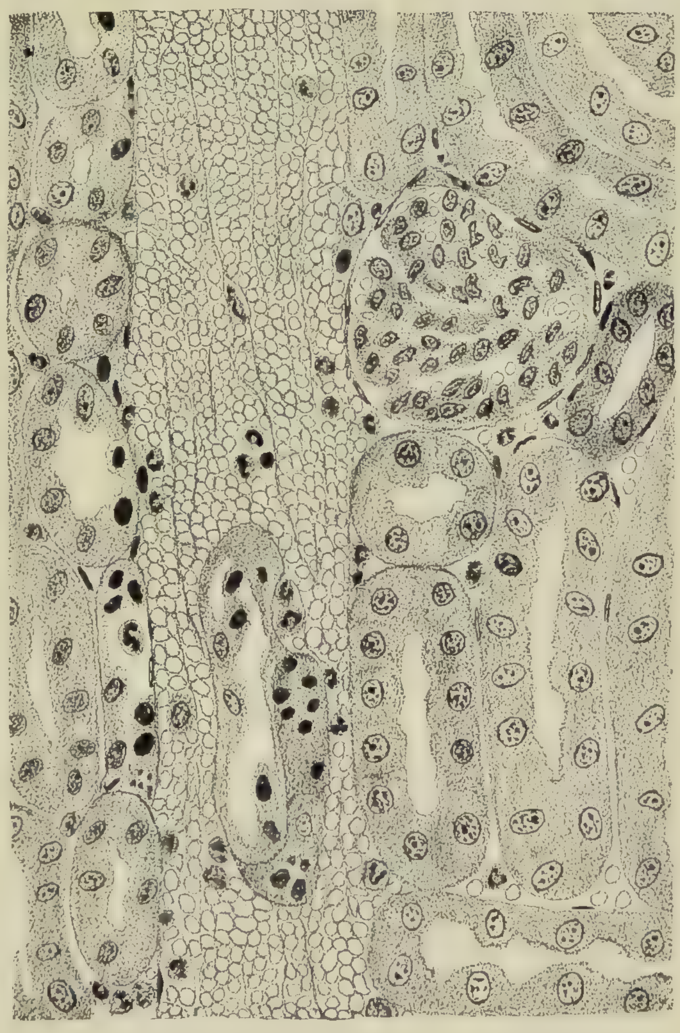

FIG. 81.—INCISION INTO THE CORTEX OF A RABBIT'S KIDNEY, MADE WITH A SHARP, THIN-BLADED KNIFE.

Specimen removed one hour after injury. The wound has been filled with clotted blood which has checked the hemorrhage. The injury to the tissues is slight and is shown by the changes in the form and the nuclei of the cells of the tubules. The nuclear network has disappeared and the characteristic morphology of the injured nuclei has been lost. They appear only as small black masses in the cells along the line of incision.

In organs possessing a glandular structure the healing process is complicated by the extensive necrosis which results from the injury to the parenchymal cells and interference with the capillary circulation supplying them with nourishment. A considerable number of these highly specialized cells die and must be absorbed before the granulation tissue with newly formed vessels can close the wound. Fig. 81 shows an incision into a kidney with the resulting destruction of tissue which illustrates this point. After the dead cells have been absorbed their place is taken by granulation tissue which ultimately repairs the injury and forms a dense cicatrix. While there may be some proliferation of the highly specialized cells of the gland, yet the amount of tissue thus produced is usually small and the growth soon ceases. Many of the newly formed cells undergo disuse atrophy later, as they are surrounded by the cicatrix and cannot perform their special function.

The methods of repair are, then: Regeneration of certain groups of cells, such as epithelium; replacement of the tissues destroyed by connective tissue; and a moderate growth of the highly specialized structures. In bone and cartilage the newly formed connective tissue undergoes metaplasia into true bony tissue or cartilage, both of which may be considered as a form of connective tissue.

CONDITIONS WHICH FAVOR AND RETARD REPAIR.

The conditions which favor and retard repair of wounds may be considered under the heads of general and local.

General Conditions.—While no doubt racial and temperamental factors play an important part in the healing of wounds it is very difficult to obtain precise figures to substantiate the belief. It is undoubtedly true that the Mongolian races and the aborigines of Africa bear extensive injuries better than the more highly organized and nervous Caucasian race, and that the differences in temperament even between the various Caucasian groups may lead to a difference in the ability to bear and repair wounds. There is no question but that in persons living an out-of-door life healing by primary union is more frequent than in the residents of cities. This, however, may not be necessarily due to the personal resistance but possibly to the smaller number of pathogenic bacteria on the skin.

Certain general diseases, such as diabetes, undoubtedly predispose to infections, especially by the staphylococcus, and the delay in healing which is frequently noted in the furuncles and gangrenous processes to which diabetics are so liable is shortened by treatment directed toward checking the disease. The frequency of terminal infections in nephritis also indicates the possibility of interference with primary repair in wounds inflicted on persons suffering from that disease. Previous acute infections, starvation, scurvy, or an acute general anemia retard the healing of wounds by reducing the reactive power of the tissues.

Wounds in infants or young persons are usually supposed to heal more rapidly than those in the aged. It is certainly known that regeneration in young people is much more active; but whether the healing process as a whole differs very greatly is still open to discussion. The most marked difference is noted in regeneration of the peripheral nerves, which is more rapid and complete in the very young.

The influence of mental conditions on surgical results has been studied by Riedel, who has shown that among imbeciles some individuals, while otherwise healthy, occasionally show diminished body activity, and that wounds in such persons heal very slowly, fractures showing imperfect union or non-union. Edema and ulcerative processes of the lower extremities are frequent. The presence of changes in the spinal cord, such as syringomyelia, could be excluded.

Local Conditions.—Local conditions which favor repair are **rest** of the injured part, a factor which is most obvious in fractures but also applies to the healing of wounds in parts where tension can be brought to bear upon the apposed edges by muscular contractions, such as, for example, transverse wounds of the anterior abdominal wall or wounds in the intestine, where the checking of peristalsis by drugs is often of great importance. The necessity of immobilizing fractures by the application of splints or of wounds by proper suturing or strapping with adhesive plaster to prevent motion is too well known to need discussion.

A proper **blood-supply** to the injured area results in more rapid healing, owing to the improved nutrition of the parts, the removal of bacteria by free exudation and phagocytosis, and the early formation of granulation tissue which checks the entrance of bacteria into the body. This increased blood-supply is aided by **warmth,** which acts by dilating the capillaries and increasing the blood-flow. While permanent chronic congestion and interference with the return of circulation delays the healing of wounds, as is well shown in chronic ulcers of the leg, yet **temporary congestion** of infected areas or slowly healing chronic inflammations has in the hands of some surgeons resulted in the rapid improvement of the condition (Bier). Whether the improvement which is noticed is due entirely to the increase of blood-flow, to the flushing of the tissues by the serum which exudes under the condition of stasis, or to the production of bactericidal or antitoxic substances in the tissues or from the leukocytes, is not yet satisfactorily determined.

Laqueur states that venous blood has a stronger bactericidal power than arterial, and that venous blood-serum obtained by congesting tissues according to Bier's method has a stronger bactericidal action than serum from the circulating blood, and that this bactericidal action plays an important part in the healing of infected tissues by temporary congestion.

Nötzel considers that the tissue juices have an increased bactericidal power when a part is congested.

A number of other factors must, however, be considered, among which are the slowing of the blood-stream, the resulting edema, and the concentration of the metabolic products of the bacteria in the diseased area. Congestion when applied to granulating wounds or sinuses causes a very marked dilatation of the delicate capillary vessels and an exudation of serum and blood from the vessels through the surface of the granulations which undoubtedly washes out the toxic products of the bacteria.

Penzo has shown that in experimental fractures in rabbits the active hyperemia which follows injury to the vaso-constrictor fibers of the sympathetic nerve-trunks favors the growth of a callus.

Under certain conditions it is of advantage to keep the surface of a wound **moist.** The best example is after a Thiersch skin-graft, where the drying of the tissues or the formation of a scab must be avoided. Sufficient moisture is obtainable by simply covering the denuded or granulating surface with gutta-percha tissue arranged in strips so as to permit of the escape of surplus exudate.

An important factor in the prompt healing of wounds is the **avoidance of infection.** Every one is familiar with the rapid healing of small clean wounds, in which union is complete in three or four days, as compared to the prolonged and tedious process seen in infected wounds.

Conditions which **retard** the healing of wounds are in many cases the antitheses of those just mentioned. Free mobility of the injured part delays union. Anemia of the tissues due to abnormal pressure of dressings, to too numerous or too tight sutures, or to the pressure of drains or contiguous bony tissues, frequently results in a local necrosis and retardation of healing. Partial or complete thrombosis of important vessels supplying the wounded area delays repair. Changes in the vessels such as are noted after burning by X-rays or radium rays are probably responsible for the extremely slow repair noted in these injuries. Arteriosclerosis and feeble heart-action, so often present in the aged, interfere with repair by diminishing the activity of the peripheral circulation. Tissues with a low vascular supply are notoriously slow in healing; good examples are the delayed union experienced in the abdominal wounds of very fat persons; in the wounds inflicted on the site of an old scar, the best example of which is perhaps the ease with which extensive ulceration can be induced on the site of an old healed ulcer of the leg by comparatively trifling injuries.

Repair is retarded by the presence in the wound of large amounts of dead tissue due to extensive trauma or foreign bodies, to heat, or to chemical action. Among the chemical necroses may be considered those produced by the use of strong antiseptics. **Cold** by contracting the vessels interferes with the healing of wounds. **Edema** is also an important factor in the prevention of rapid healing by its interference with circulation and disturbance of the tissue nutrition.

The interference with the **nerve impulses** of the part exerts an important action on the healing process, the exact method being still under discussion. Many authors hold that the slowness or absence of healing is due solely to the anesthesia of the part. Others claim (J. K. Mitchell) that the injuries to the nerves give rise to trophic disturbances producing chronic ulceration with a prolonged period of repair. Experimental section of the sciatic nerve in growing animals influences the metabolism of the limb and causes an increase in the fragility of the bone and a diminution in the volume compared with that of the other limb.

The relation of **diabetes** and **nephritis** to infection and healing has been mentioned above. **Infection** of aseptic wounds by pyogenic bacteria even in healthy persons delays healing by the toxic and destructive action of the bacterial toxins.

III. REPAIR IN SPECIAL TISSUES.

REPAIR IN WOUNDS OF SKIN AND SUBCUTANEOUS TISSUES.

The course of the healing of wounds differs according to the nature of the injured tissue, the nature of the injury, the relation of the separated parts to each other, and the processes which take place during the healing of the wound. For instance, a more complete restoration toward the original conditions of the tissues is obtained in aseptic wounds than in those which become infected, while the restoration of substance is more complete in wounds affecting tissue of the connective-tissue type than in wounds involving organs composed largely of epithelial cells.

In all cases in which the edges of the wounds are separated by considerable space or by the presence of foreign substances, such as coagulated blood or necrotic tissue, healing can take place only by the filling of the defect by new-formed tissue as the removal of the foreign substances is accomplished. The healing of such wounds, as a rule, is imperfect because the substance destroyed cannot be so completely regenerated as to regain its original structure, and the granulation tissue which unites the injured parts is finally transformed into a firm scar tissue which, although it unites the separated edges, yet does not resemble the original normal tissue. Between these extremes are many transition forms in which the results of the healing are more or less perfect restitution of the parts.

It is convenient to adopt for descriptive purposes the following traditional designations for the various types of wound healing.

1. *Primary union* or *healing by first intention*, in which the edges of the wound are directly united by a small amount of fibrinous exudate which later becomes organized by the ingrowth of connective tissue. A rapid form of repair called "immediate union" is occasionally seen in clean-cut wounds of the skin such as may be produced by a plastic operation in well vascularized areas. The healing may be quite complete in the course of a few days, but the repair is effected by the same growth of new tissue and differs only quantitatively from that type of primary union seen under ordinary operative conditions where there is considerable exudation of blood and lymph between the separated surfaces with the formation of a moderate amount of granulation tissue and complete healing only at the end of several weeks. This is the method of healing which generally obtains in uninfected wounds of the skin and subcutaneous tissues.

2. *Secondary union* or *healing by second intention* is the type of healing which is observed when the sides of the wound are not brought in direct apposition and a large amount of granulation tissue is formed before the two surfaces are united. Such wounds may heal without suppuration when not primarily infected by bacteria. If infected, however, suppuration takes place, which prolongs the course of the healing. Small wounds often unite secondarily under a crust formed by the inspissated serum and pus derived from the wound surfaces. This is usually considered as a variety of secondary union and is called *healing under a scab*.

3. *Healing by third intention* denotes the repair which takes place when

granulating wound surfaces are brought together by sutures or other means, generally after the removal of the granulations with a sharp instrument. This form of healing also occurs in abscess cavities or in sinuses healing by granulation.

Healing by First Intention.—(a) **Changes in the Wound due to Trauma.**—The immediate consequence of wounding tissues even by the sharpest instruments is the injury and necrosis of a certain number of cells along the line of the incision. This necrosis can hardly be considered as inflammatory in nature, but is due solely to the trauma. It is well seen in wounds examined within an hour after the injury and before any reaction has taken place. Degeneration of the tissue cells is noted whether blood-vessels are cut across or not. The elastic tissue and blood-vessels at the edges of the wound often retract, and there is pain, interference with function, and anesthesia or paralysis due to cutting of nerve-fibers.

The different factors vary a great deal, depending upon the nature of the wound. Injuries caused by sharp instruments may not gape open if the incision is in the direction of the skin tension. Wounds made perpendicular to the direction of tension often gape widely and have to be united by artificial means.

The second consequence of wounding tissues is the opening of lymph-channels and blood-vessels and the exudation of their contents. Occasionally we have the content of some hollow viscus extruded, as in wounds involving the intestine, stomach, bladder, etc.

The amount of bleeding which takes place depends somewhat upon the nature of the injury. It is apt to be greater when the wound is made with a sharp instrument. Crushed wounds, as a rule, bleed but slightly, and bullet wounds due to small projectiles with high velocity, as a rule, bleed very little. Wounds complicated by injury to one of the highly vascular organs, such as the liver, kidney, and spleen, are apt to give rise to extreme and often fatal hemorrhage. In wounds of the subcutaneous tissues the hemorrhage usually ceases soon after the injury, owing to the contraction of the small arteries and the formation of thrombi in the mouths of veins and capillaries.

(b) **Changes in the Wound due to Inflammation.**—About eight hours after the infliction of a so-called aseptic wound, processes begin which are designated as inflammatory and reparative. By this time the hemorrhage has ceased owing to the thrombi which have formed in the mouths of the vessels. The traumatic degeneration of surface epithelium, muscle, and connective tissue has reached its height. The line of separation between the two edges of the wound is filled with a fairly firm, adhesive clot composed of red corpuscles, fibrin, and leukocytes. By this time also softening of the fibrous tissue has begun with swelling of the nuclei of the connective-tissue cells, and very rarely mitotic figures may be found in the same. The blood-clot usually contains a few bacteria both pathogenic and non-pathogenic. These organisms are derived from the air, from the patient's skin, especially the deep layers, and possibly also from the instruments or dressings or even the hands of the operator. In the course of the next forty-eight hours the tissue reaction becomes much more marked. Numerous mitotic figures are found in the surface epithelium and in the connective tissue. The blood-vessels are dilated and the formation of granulation tissue has reached considerable proportions, the fibroblasts accompanied by delicate capillaries passing into the clot which unites the wound. Numerous phagocytic cells, either of the giant cell type or belonging to the leukocyte or endothelial groups, are present in the depth of the wound. Usually by the end of four days the epithelium has covered the surface of the wound, while the granulation tissue has nearly or completely replaced the blood-clot, both conditions depending somewhat upon the closeness of apposition of the wound edges. By the sixth or seventh day the blood-clot has completely disappeared and has been replaced by a very cellular and vascular tissue. No bacteria can be found in cultures made at this time from such a wound. They have been either destroyed by the bactericidal action of the serum of the exudate or engulfed by phagocytes. By the end of three weeks the granulation tissue has been entirely transformed into a dense fibrous scar containing but few nuclei. Here and there may be seen remnants of the sweat and sebaceous glands and occasionally small islands of epithelium. The glands usually are capable of regenerating their excretory ducts, but they may also atrophy or form small cysts. The epithelium in the depths of the wound may form a so-called implantation dermoid or be destroyed by phagocytes and tissue ferments.

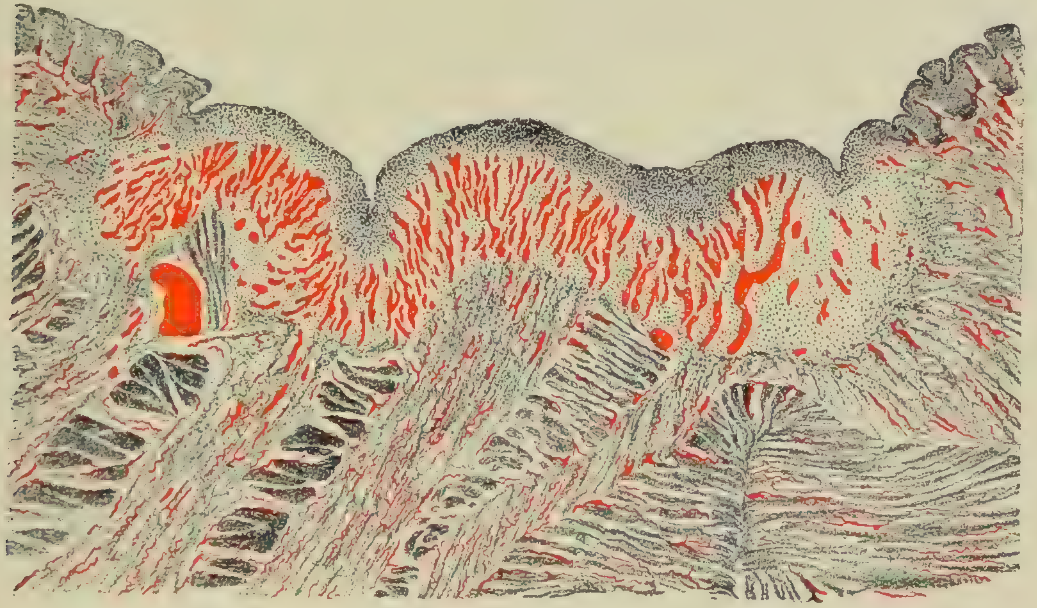

FIG. 82.—GRANULATING WOUND IN DOG'S TONGUE INJECTED FIVE DAYS AFTER INJURY.

On either side of the drawing may be seen the uninjured epithelial layers, while between them lies an area with an irregular surface. The upper portion of this mass is composed of leukocytes, the lower of very vascular new connective tissue. At the periphery may be seen the muscle fibers and blood-vessels as normally present in a dog's tongue. The striking feature is the extreme vascularity of the granulation tissue.

Healing by Second Intention.—If an open wound, protected as far as possible from drying, is examined at the end of twenty-four hours, the edges of the skin about it will be noted to be red and swollen, and the depth of the wound to be covered with a layer of serum and fibrin of a reddish or yellowish color from admixture with emigrated leukocytes and red cells. Microscopically, the tissue exposed by the injury will be found to have undergone necrosis due to trauma, to interference with the capillary circulation, and to the action of the air which irritates the raw area and, by aiding evaporation, alters the osmotic balance between the tissues and the fluid bathing them. The tissues in the neighborhood of the wound are infiltrated with red and white blood-cells and the vessels are surrounded by emigrated leukocytes. At the end of forty-eight hours, the raw surface assumes a jelly-like appearance; it is difficult to recognize the different tissues exposed; and the color is less reddish and has assumed a grayish tint. If carefully examined, the surface of the wound may show small, reddish elevations, which by the end of the third day usually fuse to cover the entire surface. These "granulations" are red, the color being due to their extreme vascularity. The irregularity of the surface depends upon the presence in each granulation of a tuft of new-formed capillaries accompanied by more or less connective tissue (Fig. 82). Such a wound exudes a serous or purulent fluid from the surface, which consists of serum, fibrin, leukocytes, and red cells. Attached to the surface of the granulations is a thin layer of fibrin containing large numbers of entangled leukocytes. Smooth, compact, reddish granulations are designated clinically "healthy" granulations or "normal" granulations.

Under unfavorable local conditions or in persons whose resistance is diminished by prolonged illness the granulations may assume a different type. In some cases the surface is very irregular and the projections are soft and bleed upon the slightest touch, and are also extremely sensitive to contact with foreign material, such as dressings, or any irritating substance. This form of granulation tissue has been called "irritable" granulations or "erethistic" granulations. Such granulations do not, as a rule, lead to prompt healing, and necessitate active treatment in order to stimulate the growth of a normal type.

Another form of granulation tissue differing from the healthy is that known as "exuberant" granulation tissue. This form, instead of being firm to the touch and reddish in color, is pale and shows an irregular, soft, spongy surface. Such granulations are usually covered by a thicker layer of yellowish, fibrinopurulent exudate than under more healthy conditions. Through this yellow layer project small reddish points which indicate more rapidly growing and vascular areas in the tissue.

Granulations are also seen which may be called "diphtheritic" granulations, a term denoting the thick fibrinopurulent exudate overlying the granulation layer of cells and blood-vessels. Inasmuch as the term diphtheritic is now used to designate an exudate due to a specific microörganism, it is better to employ the name "croupous" or "pseudo-membranous" for this form of granulation tissue. This pseudo-membranous type is not often seen and is suggestive of tuberculosis or of a syphilitic infection of the wound surface; but microscopic examination often shows that neither of these two agents is concerned in the process.

There is another variety of granulation tissue in which the structures are altered by the specific action of the poisons of tuberculosis and syphilis. Tuberculous granulations are usually of the flabby, pale, exuberant type, and when examined microscopically show the characteristic lesions incited by the tubercle bacillus. The tubercles are usually more or less necrotic in their centers and may show abundant giant and large flat cells about the periphery. Syphilitic ulcerations are often covered by pale, flabby granulations, though occasionally they may assume a type which closely resembles normal, healthy granulation surfaces. Microscopic examination, however, will usually reveal the characteristic lesions of syphilis, which are areas of necrosis with a few giant cells scattered through the tissues, swelling of the endothelium of the capillaries with a perivascular infiltration of leukocytes, usually mononuclear in type.

A wound covered by healthy granulations usually tends progressively toward healing by the filling up of the denuded area by the continuous growth of granulation tissue, and by the covering of the surface of these granulations with epithelium extending in from the edges of the wound. Other types of granulation tissue usually require treatment or removal to enable the wound to heal properly. Syphilitic granulations often respond only to treatment with mercury and an iodid.

The microscopic details of the process which goes on during the formation of granulation tissue are as follows: The surface of the fresh wound is covered with a layer of fibrin formed from the exuded blood-plasma. Necrotic epithelium, muscle cells, and other products of the traumatic action of the agent producing the wound, lie under this layer. The bundles of connective tissue of the subcutaneous tissue are separated from each other by blood and serum; the bodies of the cells between the bundles enlarge and the nuclei proliferate. Numerous leukocytes, chiefly of the neutrophile variety, infiltrate the tissues. The vessels give off thin-walled capillaries which grow out into the soft mass of new-formed cells springing from the edges of the wound. Necrotic muscle fibers or other tissues are absorbed by phagocytes.

The cells contained in granulation tissue are derived partly by mitotic division of the preëxisting cells of a connective-tissue type forming the boundaries of the wound, and partly from the cells emigrating from the blood-vessels. The actively growing, young connective-tissue cells are usually designated as fibroblasts. These are irregular, spindle-shaped, or spheroidal cells with a large nucleus which often shows the varying phases of mitotic division (Fig. 83). The resting nucleus is usually vesicular, in distinction to the compact nucleus of the leukocytes and other wandering cells (polyblasts). When the fibroblasts assume a spheroidal form they are often designated "epithelioid" cells, from their resemblance to epithelium.

The fibroblasts of healthy granulation tissue at first lie in a jelly-like stroma showing practically no structure except interlacing strands of fibrin. As the healing process continues and the cells mature, fibrils develop either in the cell-body, or, as some believe, in the intercellular substance. The fibrils gradually increase in number and the fibroblasts diminish in size, and finally can be seen in the cicatrix only as long, slender cells, often lying in clefts between the fibers of the firm connective or scar tissue.

The **leukocytes,** so abundantly present in granulation tissue, are the same as those of the circulating blood. All varieties of leukocytes leave the vessels and appear in the tissue, but as the polynuclear cells with neutrophile and eosinophile granules possess the power of active ameboid movement to a much more marked degree than the basophiles (mast cells) and lymphocytes, a larger proportion of the first-mentioned cells are found in the tissue under consideration. Usually the polynuclear neutrophiles outnumber very considerably all other varieties of leukocytes, not only owing to their relative preponderance in the blood, but to the positive chemotactic action exerted by many of the pyogenic organisms which are often present on the surface of a granulating wound. The non-granular lymphocytes, however, appear in the tissues in moderate numbers, especially in syphilitic inflammations in connection with numerous plasma cells, while in certain chronic inflammatory conditions the basophile cells often appear abundantly. Maximow, who has studied with great care the character of the cells in inflammation, considers the large and small lymphocytes as very important in the process. These cells form a large proportion of the wandering cells which he terms polyblasts, and he includes with the same group mononuclear polyhedral cells derived from the adventitia of the blood-vessels and from the preëxisting wandering cells of the tissues.

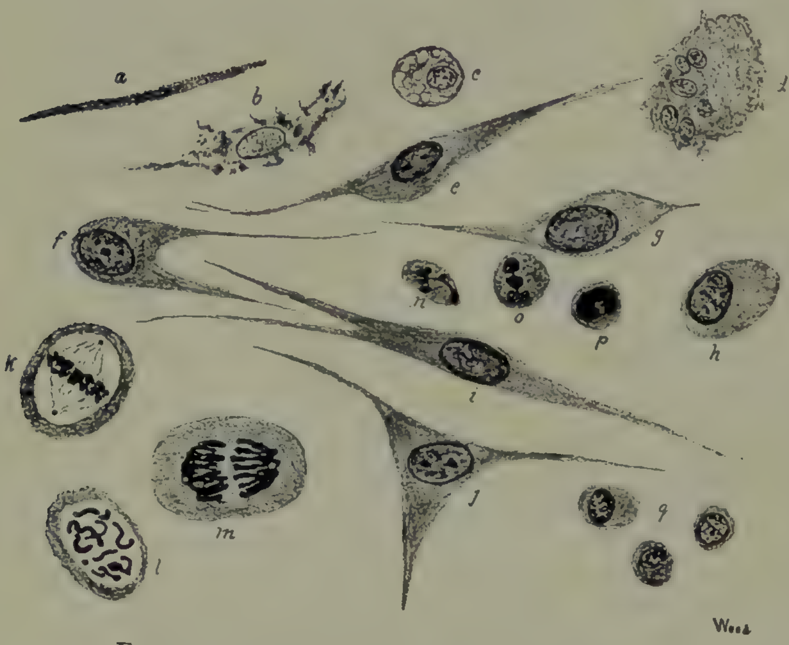

FIG. 83.—CELLS FROM GRANULATION TISSUE.

a and *b*, Clasmatocytes; *c*, vacuolated and fatty connective-tissue cells; *d*, giant cells: *e*, *f*, *g*, *h*, *i*, *j*, various forms of fibroblasts; *k*, *l*, *m*, phases of mitosis in connective-tissue cells; *q*, three plasma cells.

The group of wandering cells known as **plasma cells** has been much studied of late years, chiefly in connection with chronic skin diseases and syphilis, such cells being especially abundant about the blood-vessels in the latter condition. While it is generally held that they are derived from the fixed tissue cells, some observers hold that they are merely lymphocytes transformed after their emigration from the blood-vessels. The morphology of the plasma cells seen in granulation tissue is quite variable. They may be either round or spindle-shaped, and occasionally they assume a very irregular outline with long projecting fibers. The nucleus is usually single and oval. The chromatin network is thick and heavy, like that of the lymphocytes (Fig. 83, *q*). The cell-body stains dark blue with methylene-blue and shows a granular structure with sharply defined granules such as are seen in mast cells. Mitoses are infrequent, but evidences of direct division are often met with. They do not act as phagocytes (Councilman).

It has been asserted that the endothelial cells of the lymph-spaces and blood-vessels may be set free during the growth of the granulation tissue, and act as phagocytes. Large cells are not uncommonly present which are either endothelial in origin or derived from connective-tissue cells (macrophages). Their phagocytic power is very great, and foreign bodies, leukocytes, and red corpuscles are not infrequently found embedded in their cytoplasm.

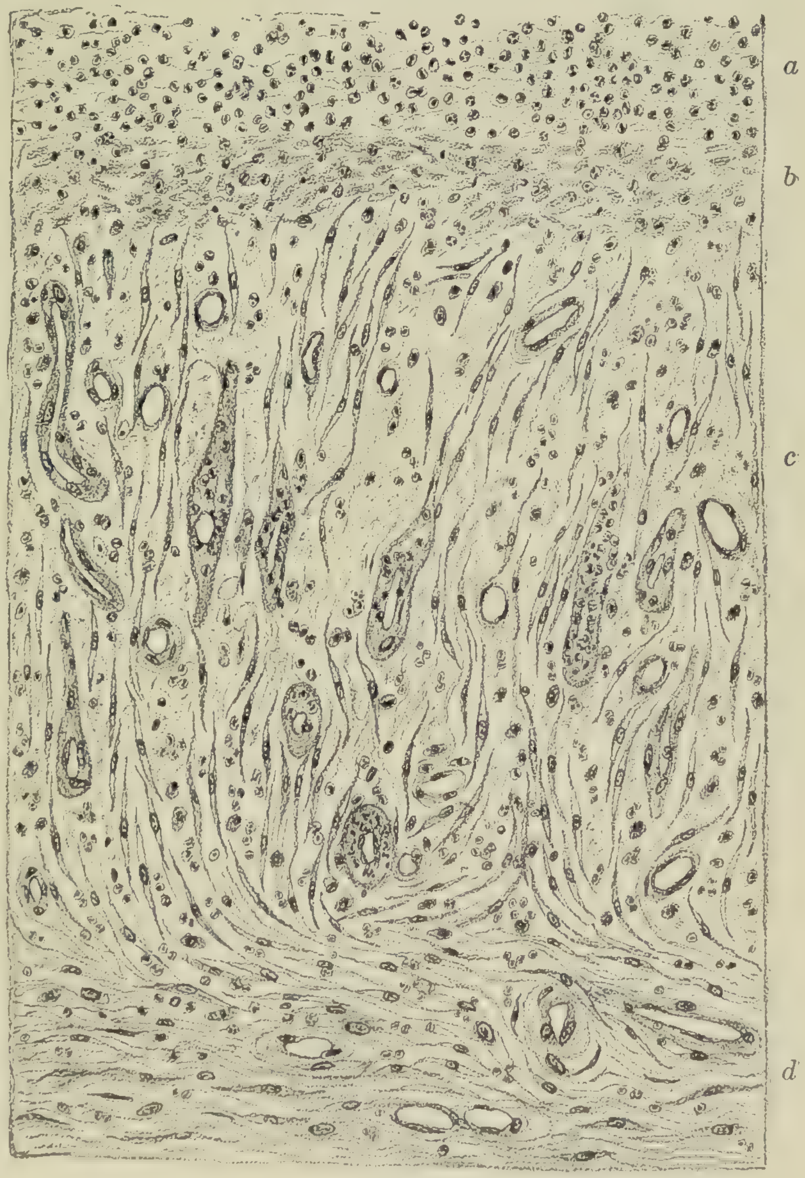

Fig. 84.—Granulation Tissue.

a, Layer of fibrin and leukocytes; *b*, layer of leukocytes and necrotic cells; *c*, granulation tissue showing fibroblasts and blood-vessels; the blood-vessels are surrounded by a large number of plasma cells and leukocytes; *d*, firm connective tissue from which the granulation tissue springs; this firm, fibrous tissue contains only a few cells and thin-walled blood-vessels.

Among the cells found in small numbers in the later stages of granulation tissue and also in scars, are the **clasmatocytes**, first described by Ranvier. They are large, spindle-shaped, or branching cells with an irregular nucleus and a body protoplasm containing metachromatic granules. It is probable that the clasmatocytes of the tissues include the group of cells found in the blood and designated mast cells by P. Ehrlich. They only rarely act as phagocytes (Fig. 83, *a* and *b*).

Giant cells are also found in moderate numbers in granulation tissue. They are formed by fusion of the endothelial or proliferation of the connective-tissue cells, or by division of the nucleus of the cell with increase in the size but without separation of the body. Muscle cells not infrequently form multinuclear cells resembling giant cells in inflamed tissues. Such cells are most abundant in granulation tissue which contains foreign bodies, especially suture material (Fig. 83, *d*).

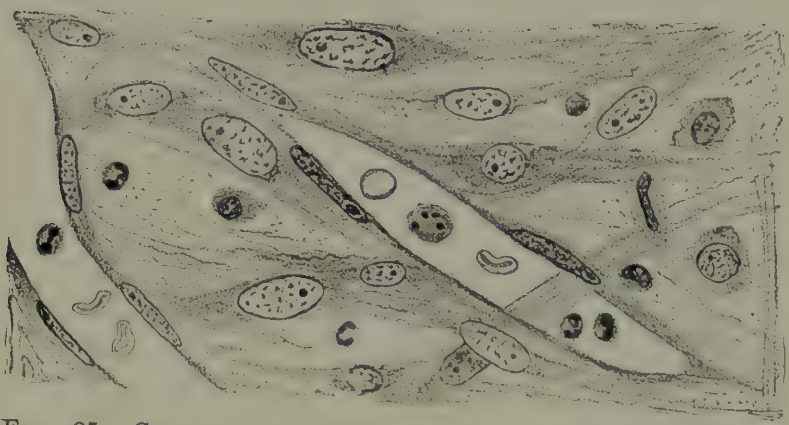

Fig. 85.—Granulation Tissue from Laparotomy Wound showing Thin-walled, Newly Formed Vessels, Fibroblasts, Leukocytes, and Plasma Cells.
The formation of connective-tissue fibrils may be noted in the bodies of the fibroblasts.

The **blood-vessels** in the granulation tissue are formed by sprouts from those preëxisting in the tissues but severed by the trauma which gave rise to the wound. The endothelial cells of the walls of the vessels give off long projections occasionally terminating in a knob-like end. These strands of cells are usually considered to be at first solid, later to become hollowed out and form a channel for the passage of the blood. Maximow, however, states that the sprouts are hollow from the first (Figs. 85, 86, and 87). This new formation of vessels takes place rapidly and abundantly in granulation tissue, which is therefore filled with a close meshwork of thin-walled blood-vessels. In exuberant granulations the walls remain thin, which accounts for the ease with which bleeding may be produced; and the vessels are often

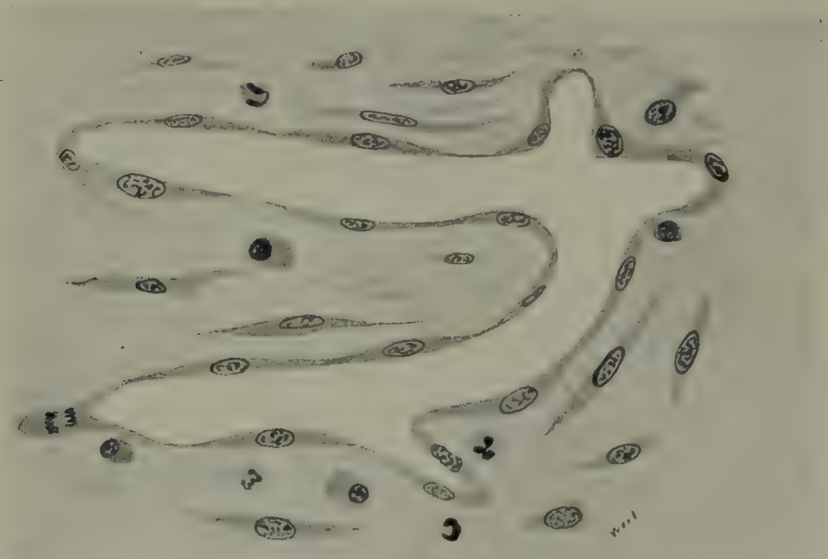

Fig. 86.—Thin-walled Capillary from Granulation Tissue showing the Budding of the Endothelial Cells.

unusually abundant and not surrounded by the regular amount of connective tissue. In a healthy form, however, the vessel wall soon thickens by the growth of adventitial cells, some of the type of connective tissue, others of the plasma-cell group (Fig. 88). As the fibrous tissue becomes older and more dense, the vessels become obliterated and the scar paler than the nearby healthy tissues.

Elastic fibers only appear in newly formed connective tissue in the later stages of the healing process. Fine fibrillæ may be seen projecting from the older, thick strands of elastic tissue of the original tissues at the edges of the wound. It is not as yet definitely known whether the fibrils are derived only from the older strands of elastic tissue or from the bodies of cells, as are the fibers of the connective tissue, or whether they are due to a further differentiation of the fibrillar connective-tissue stroma. Collections of elastic tissue develop most abundantly about the new-formed blood-vessels and under the surface of the regenerated skin covering the site of the injury.

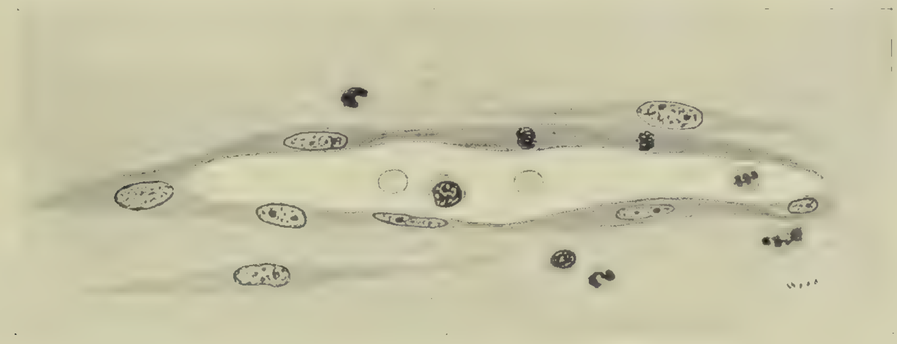
Fig. 87.—Thin-walled Capillary from Granulation Tissue showing the Relation of Leukocytes and Fibroblasts to the Wall of the Vessels.

The **epithelial cells** near the edges of a traumatic wound show the evidences of degeneration which have been previously mentioned on page 362. Eight to ten hours after the infliction of the injury the epithelial cells swell, the nuclear chromatin thickens, and a few mitoses can be found as an evidence of beginning multiplication of the cells. This division takes place chiefly in a lateral direction, so that the chief growth of the epithelium is parallel to the surface of the wound, the newly formed cells extending out over the injured area.

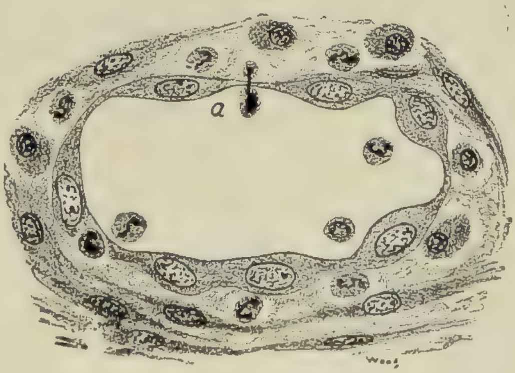

Fig. 88.—Capillary from Granulation Tissue showing Adventitia Cells Surrounding it and at *a* a Leukocyte Emigrating from the Lumen.

In narrow, shallow, incised wounds, the epithelium fills up the cavity very promptly (see under Healing by First Intention and Healing of Corneal Wounds), and very small superficial incisions may be closed in twenty-four to forty-eight hours, by the new growth of the epithelium. Larger wounds require a much longer period of time. The healing of a very large granulating area may require months for complete repair, unless the process is aided by skin grafting.

If the edge of a granulating wound is carefully examined four or five days after the injury, it will be seen to be bordered by a thin, bluish-white layer, which is the newly formed projection of the epithelium. This layer may be only a few cells thick and is occasionally irregular in outline and shows small projections of granulation tissue appearing through the surface. This newly formed epithelium adheres to the surface with some firmness, but can be rubbed off by rough treatment with instruments or by the application of dry gauze dressings, which when removed take off some or all of the newly formed epithelial cells.

Vertical sections through the periphery of such a healing wound show that the outgrowing epidermis does not form a wedge-shaped projection, but that the advancing border is usually slightly thickened. It is often, however, very difficult to determine the exact point of extension of the epidermis, because the cells mix with the fibroblasts of the granulation tissue and the exudate of leukocytes or fibrin on the surface, so that differentiation of the various types may be impossible.

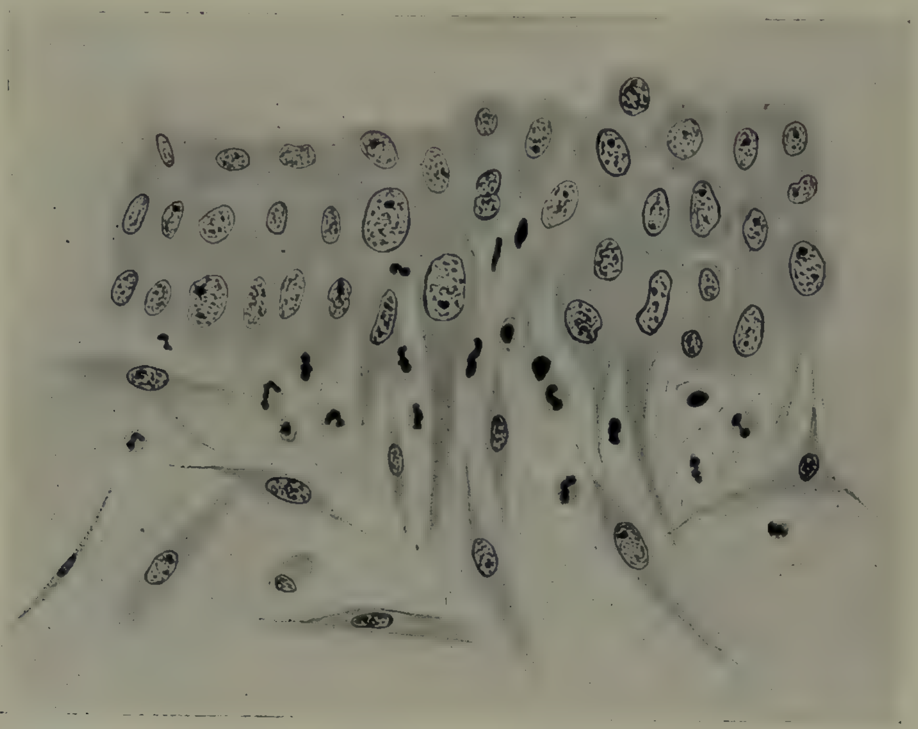

FIG. 89.—GROWTH OF EPITHELIUM ON SURFACE OF GRANULATION TISSUE SHOWING THE EXTENSION DOWNWARD OF SPINDLE-LIKE PROJECTIONS FROM THE EPITHELIAL CELLS.

The epithelial cells frequently project downward between the fibroblasts or send short projections of groups of cells into the tissue (Fig. 89). Such projections lie between the tufts of capillaries supplying the individual granulations, so that the epidermal surface follows the lobulations of the granulation tissue. The cells near the edge of the ingrowth are irregular in shape and often give off small projections through wide intercellular spaces (Fig. 90). The cells of the superficial layer are flat, with smaller nuclei than those below, while at a short distance from the free border of the epithelium these flattened cells may show evidences of cornification. The nuclei of the epithelial cells are often lobular or double, a phenomenon probably indicating direct division. Mitoses are usually absent in the immediate vicinity of the advancing edge, but abundant in the cells of the lower layer some distance from the border of the wound. After the epithelial layer has assumed a thickness of six or eight layers of cells the boundary between it and the fibroblasts is much better marked than previously (Fig. 91), and evidences of a sort of basement membrane may be seen. The lower cells are usually cylindric or cubical, in contradistinction to the flattened superficial cells, and mitoses are abundant. Leukocytes are not uncommonly inclosed in the bodies of the epithelial cells or lie between them (Figs. 90, 91, and 92).

When the surface of the granulating area is finally wholly covered with epithelium the production of exudate ceases and the progressive inflammatory processes are followed by regressive changes. The granulation tissue loses its extreme vascularity; the bodies of the connective-tissue cells become smaller; while the amount of fibrous tissue increases and a cicatrix is gradually formed. Further details of this transformation will be found on page 374.

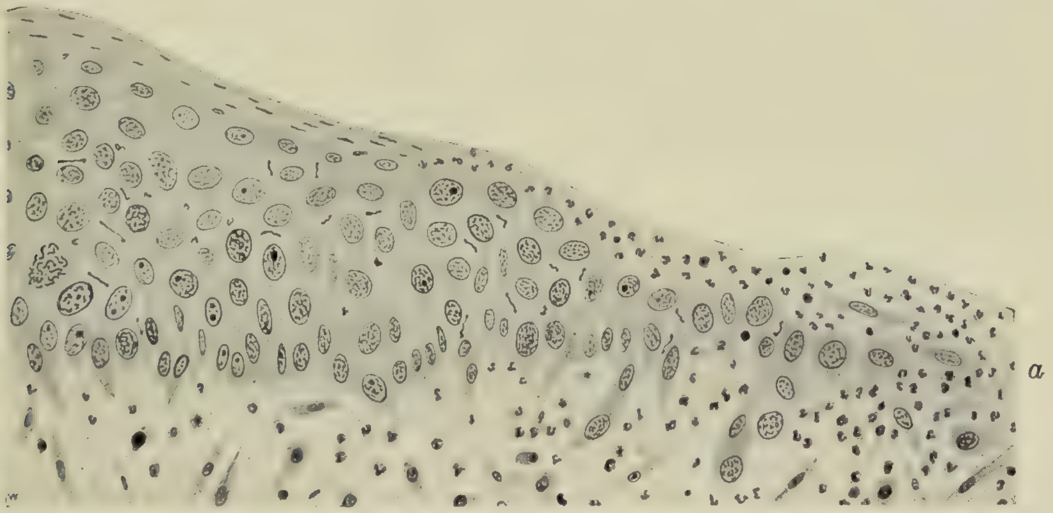

FIG. 90.—SECTION SHOWING THE ADVANCING EDGE OF EPITHELIAL NEW GROWTH OVER A GRANULATING SURFACE.

The epithelial cells at the advancing edge (at *a*) are scattered through the tissue and can scarcely be distinguished from fibroblasts.

In infected subcutaneous wounds or abscesses the inflammatory reaction following the injury to the tissues by the bacterial toxins induces the formation of granulation tissue. While the process is active the destructive effects are more marked than the reparative and the so-called abscess membrane is usually composed chiefly of a thin layer of proliferating connective tissue containing many phagocytic cells and leukocytes, and a much thicker layer composed of fibrin, leukocytes, and necrotic tissue cells. The granulation tissue and the connective tissue beneath it are apt to contain a very much larger number of polynuclear leukocytes than the ordinary healthy granulations of a healing wound. If untreated, such an abscess may not heal for a long time. When such an abscess is drained, however, and free exit is given for the discharge of the pus, débris, bacteria and their products, a more healthy growth of tissue begins which usually results in prompt closure of the cavity. The slough on the surface of the granulations is chiefly removed by autolytic processes, the ferments being derived from the cells of the rapidly growing healthy granulations. Occasionally, especially in infections of the female generative organs and of the liver, the abscess may in time become free from viable bacteria, and under these conditions a more healthy production of granulation tissue may be noted. Such granulations are apt to show a more marked capillary development than those which appear on the free surface, where the delicate loops of capillaries lack the support which is given them by the fluid of the abscess (Fig. 93). In a small abscess the pus is occasionally absorbed and the cavity closed by granulation and, ultimately, scar tissue without opening the cavity, but this is rare. Abscesses which have become sterile, such as are seen frequently in connection with the suppurative inflammations of the Fallopian tube, may finally contain only a cheesy mass of dead leukocytes and tissue cells. Such masses of débris may occasionally become infiltrated with lime salts and form calcareous nodules.

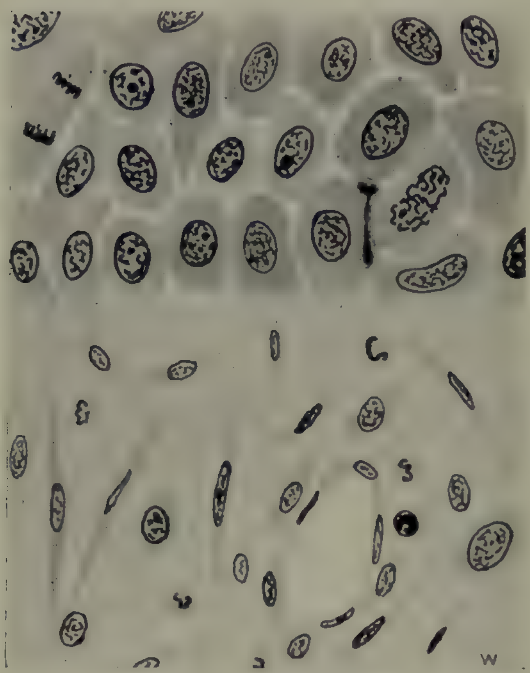

Fig. 91.—Section taken at Some Distance from the Advancing Epithelial Edge of a Granulating Wound.
The boundary between the epithelium and the connective tissue is well marked.

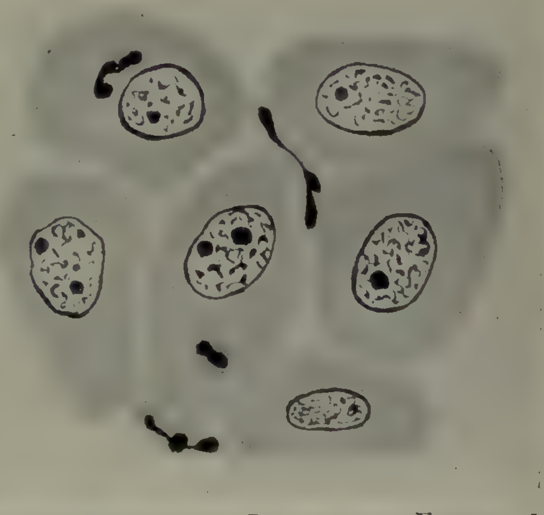

Fig. 92.—High-power Drawing of Epithelial Cells showing Leukocytes in and between the Epithelium.

In the so-called cold or tuberculous abscesses, inasmuch as the action of the tubercle bacillus is chiefly to incite necrosis, we find but little granulation tissue in the walls and a thick abscess membrane of fibrin and dead cells. The fluid which fills these tuberculous abscesses is usually designated pus, but it differs from the pus of a fresh abscess in that a large majority of the cells have undergone advanced degenerative changes, while the leukocytes of pus from an acute inflammation due, for example, to the staphylococcus, are many of them alive and actively motile. The bodies of the cells in a tuberculous abscess are frequently filled with fat granules or are vacuolated.

Such granulation tissue is apt to contain a considerable number of tubercles with cheesy centers and giant cells. These tuberculous granulations are usually flabby and pale, and in order to obtain a healthy repair of tissues it is necessary to scrape out all the tuberculous tissue lining the sinus or the cavity, and especially to remove any irritating substance deep in the tissues, such as a small bone sequestrum.

Healing by Third Intention.—The healing by "third intention" of the older writers denoted the union of two granulating surfaces. The general use of the method of repairing extensive wounds by suturing after granulation tissue had formed and the extensive discharge of pus had ceased, was necessitated by the difficulty of obtaining clean wounds which would heal directly. Since the introduction of aseptic methods the use of the method of union by third intention has practically disappeared from surgical technic, except in the healing of small granulating abscesses or sinuses. At the present time deep granulating wounds are sutured only after thorough removal of the granulations and irrigation of the cavity, thus uniting the original tissues under the granulations by first intention.

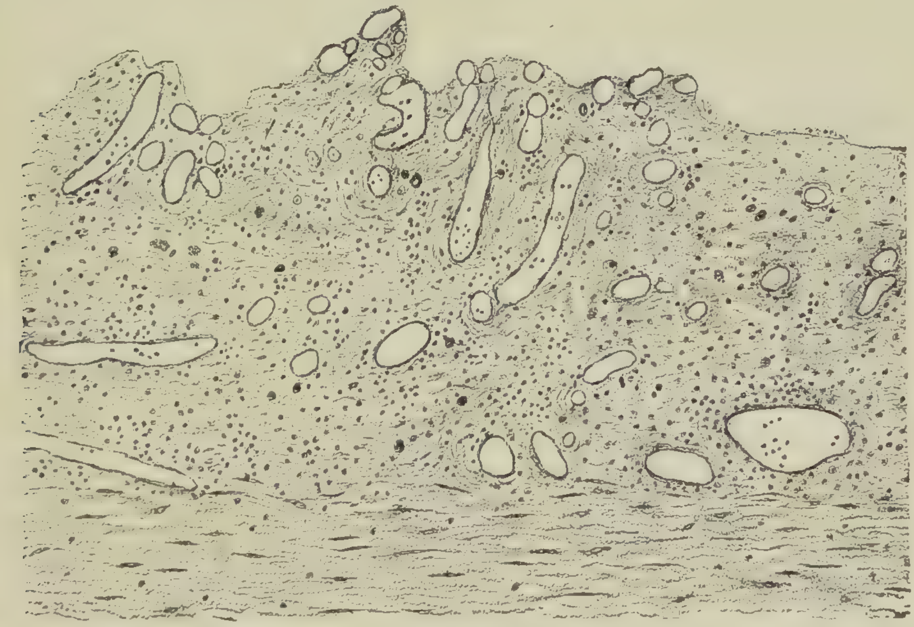

FIG. 93.—GRANULATION TISSUE FROM AN ABSCESS CAVITY SHOWING MARKED DEVELOPMENT OF THIN-WALLED CAPILLARIES.

The healing of abscesses and sinuses is accomplished, first, by falling in of the tissues so that the walls may be in more or less close apposition after the fluid which has distended them is removed, and, second, by the natural contraction of the cicatricial tissue formed during the granulating process. When the granulations, by their growth, come in contact, the connective-tissue structures unite and the sprouting blood-vessels pass from one side to the other, union in this case being a simple fusion. The details of the process are the same as those described under healing by second intention.

Cicatrization.—If a fresh wound is examined shortly after the injury, the dimensions will be noted to be greater than during or after healing. This is due to the retraction of the edges primarily produced by the elastic nature of the tissues. As the process of repair continues the area becomes smaller and finally the regeneration of the epithelium begins. After the surface of such a granulating wound is completely covered by the ingrowth of epithelium from the edges, or by skin grafting, certain changes begin in the granulation tissue which has been recently covered by epithelial cells and is still very vascular. These changes are termed scar formation or cicatrization.

In wound healing by primary intention the amount of new tissue formed is so small that a clinically well-marked scar is not formed, though microscopically the same changes may be ultimately observed as take place when a large area is denuded. These changes concern chiefly the fibroblasts and the blood-vessels. The fibrillæ of connective tissue increase in number at the expense of the cytoplasm of the fibroblasts, and finally the latter are so altered that they appear only as narrow, flattened nuclei, lying between dense bands of connective tissue. The leukocytes and other wandering cells disappear with the exception of a few clasmatocytes which persist for a long time. The numerous blood-vessels which exist in the granulation tissue undergo regressive changes due perhaps to the contraction of the connective tissue, so that the scar, though originally of a deep red color, becomes quite pale, much more so than the surrounding skin. The irregular surface of the granulations, as previously stated, corresponds to the arrangement of the blood-vessels, and the newly formed epithelium of the cicatrix follows this irregular surface to a certain extent, and sends small projections of epithelial cells down between individual granulations. The final result is that the surface becomes smooth; the granular surface and the epithelial projections flatten

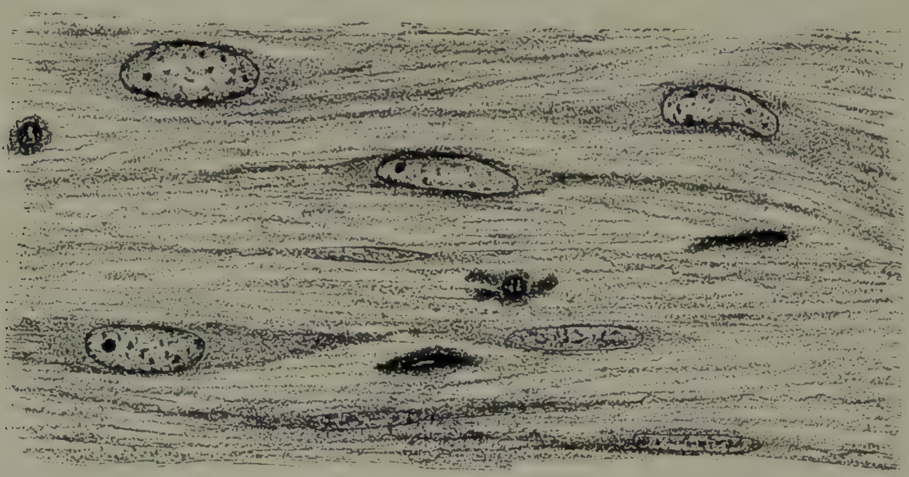
FIG. 94.—SCAR TISSUE FROM A HEALING WOUND OF TWO WEEKS' DURATION. Showing the formation of fibrils in the bodies of the fibroblasts. A few leukocytes, clasmatocytes, and plasma cells remain in the interstices of the tissue.

out; hair is usually absent; the sweat and sebaceous glands are present in moderate numbers or entirely absent. The epidermis formed is usually much thinner than normal and has a white, polished look which is characteristic. The regular furrowing of the normal skin is not reproduced, as is best shown in wounds of the palmar surface of the fingers.

The consistence of the scar is much firmer than that of normal skin, as would be expected from its densely fibrous nature and the absence of the usual subcutaneous fat. Even small furuncles may leave a hard, irregular nucleus in the subcutaneous tissues. When the scar is adherent to the underlying muscles and fasciæ it is quite immobile.

The new formation of elastic tissue fibers takes place only some months after the healing of a wound. According to our present knowledge, they extend from the old elastic strands left in the edges of the wound, and are much finer than the normal fibers. The pigment of the skin in scars is usually much less well marked than in the normal. Scars in the negro show much less pigmentation than the rest of the surface. Nerve fibers are scanty or absent.

Scars with thin epidermis are very sensitive to trauma, and the surface may become very rapidly denuded after an injury which would not affect a well-nourished tissue. Scar tissues are characterized by their great tendency to retraction. This is least noticeable in linear incisions which have healed by primary union and greatest in broad, deep scars seen, for example, after extensive burns involving all the layers of the skin. The amount of contraction is dependent upon the area denuded and the slowness of the repair; in other words, on the amount of granulation tissue produced. This explains the great value of early skin grafting after extensive denudation, as after amputation of the breast. The consequence of the retraction is that in the course of time the scar area becomes thinner and smaller than the original wound surface and large scars often interfere greatly with the movement of the extremities owing to the inelasticity of the cicatrix. After a year or two the scar tissue may become somewhat more elastic, and it is possible to stretch the cicatrix by constant exercise so as to diminish somewhat the functional defects produced by the contraction.

The above description applies to wounds of the skin and subcutaneous tissues. Scars in other localities are of much less clinical importance. Those produced by subcutaneous wounds are small; those in organs do not, as a rule, interfere very greatly with the functional efficiency of the uninjured tissue which remains. Only in the gastro-intestinal tract are extensive cicatrices important. The contraction of healing ulcers of either the stomach or the intestine may lead to stenosis of the lumen, that of peritoneal adhesions to strangulation of the included gut. The histologic changes are very similar to those described above; that is, an alteration of the structures repairing the injured area into dense connective tissue.

Healing under a Scab.—The process of repair of wounds under a dry crust or scab has many similarities to repair by granulation. It is really a type of healing by second intention. While its importance as a means of procuring satisfactory repair of wounds has been diminished by the introduction of aseptic methods, interest has recently been attracted to this means of healing by the observation that many gunshot wounds produced by modern high-velocity projectiles heal most satisfactorily when the wound is allowed to dry under a primary aseptic dressing. A large proportion of uncomplicated gunshot wounds will heal smoothly by this process, as the small-caliber mantled projectiles now in use are not apt to carry fragments of cloth or other foreign bodies into the depth of the wound, a condition which is frequently noted after injury with the old, large-caliber lead bullets. Other wounds than those produced by bullets may heal satisfactorily under a scab; for example, injuries following the action of strong chemicals such as carbolic acid; burning with hot metal; and some types of limited gangrene. Practically all of the small cuts and scratches occurring in daily life heal under a scab.

The phenomena observed in this form of repair are merely a modification of those seen in healing by granulation as previously described. The denuded area is covered with a crust composed of dried serum, red and white blood-corpuscles, fibrin, and tissue detritus. This rapidly dries and forms a protective coat under which a moderate amount of granulation tissue forms, usually without any large amount of inflammatory exudate. The necrotic tissues beneath the crust are removed by absorption and phagocytosis. The products of the regeneration of the connective-tissue cells fill up the cavity produced by the trauma, while the epithelium grows under the scab in a manner similar to that observed in the healing of skin grafts. If the wound is superficial, the remains of the ducts of the sweat or sebaceous glands and the hair-follicles furnish epithelium which by its proliferation forms small islands of cells, thus hastening the coating of the surface with epithelium. As soon as the loss of the epithelium has been completely repaired the scab can be separated from the surface of the wound, leaving behind it the new-grown skin. This has the same texture as is noted in other wounds; the epithelial layer is thin and does not show the rugæ seen in normal skin; the hair-follicles and the cutaneous glands are usually missing or present only in small numbers when the loss of substance has been considerable.

Healing of Subcutaneous Wounds.—Wounds of the subcutaneous connective, fatty, or muscular tissues may be produced by external violence. Usually such wounds remain uninfected by bacteria, and repair is accomplished by the growth of a small amount of new connective tissue from the cells surrounding the injured area, the exudate and extravasated blood being absorbed by the blood- and lymph-currents or carried off by phagocytes. The pigment of the blood is dissolved from the corpuscles and altered into hematoidin, a substance closely resembling, if not identical with, bilirubin. Phagocytic cells bearing particles of such pigment remain for a long time about the periphery of a subcutaneous hemorrhage.

If the extravasated serum and blood become infected, the abscess so formed may discharge its pus through a sinus leading to the surface of the body or into a hollow viscus, healing following by the formation of granulation tissue which fills the contracting cavity. In small abscesses healing is occasionally seen by a process of absorption of the pus and filling of the cavity by granulation tissue after the acute inflammatory stage has passed. The bacteria are destroyed by the action of the exuded serum or removed by phagocytes. Imperfect resorption of the pus may be followed by calcification of the débris remaining in the cavity.

Healing under Blood-clot.—While it is generally preferable in the treatment of wounds to close the adjacent surfaces so tightly as to leave little or no space for the collection of fluid, yet occasionally this is impossible. The tissues may be separated by so considerable a distance that it is impossible to approximate them by pressure or sutures without running the risk of necrosis of the wound edges owing to compression of the vessels and destruction of the cells. Cavities in rigid tissues, such as bone, cannot always be closed so as to avoid a dead space. Under these circumstances it may be proper in uninfected wounds to allow the cavity to fill with blood which ultimately coagulates and forms a supporting framework for the growth of granulation tissue which springs from the walls of the space.

Infected wounds cannot be treated in this manner because of the danger of a very violent inflammatory reaction being set up in the wound due to the fact that the coagulum acts as a culture medium for pathogenic bacteria. In case such infection occurs it is necessary to drain the wound and allow it to granulate. As, however, an absolute asepsis is practically impossible, the presumption is that the bactericidal action of the blood-serum of the clot is capable of rendering innocuous a certain number of bacteria in those cases in which healing occurs without symptoms of infection.

The microscopic details of the healing process are as follows: Granulation tissue is formed at the periphery of the wound and gradually extends into the cavity. The clot is softened by the action of ferments given off from the leukocytes and the tissue cells, and is finally removed by phagocytic leukocytes or tissue cells, as the granulation tissue fills the cavity more and more. When the dead space has been completely filled by granulation tissue the usual changes occur in this substance, resulting in the formation of a firm fibrous cicatrix.

Cavities in bone occasionally do not heal under a blood-clot, as the vascularity of this tissue is not always sufficiently great to permit of an active formation of granulations. Such cavities may remain filled with fluid blood for several years even though complete closure of the skin wound has been obtained, and are always a menace to the health of the patient from the risk of infection of the fluid remaining in the cavity.

Under these conditions it has recently been suggested (Mosetig-Moorhof) to fill the cavity with a mixture of iodoform and wax, on the same principle that teeth are filled in dental practice. Healing about the foreign body takes place, but without any active reparative growth in the bone.

Skin Grafting.—The covering of large areas denuded of skin is a problem which often presents itself to the surgeon, either after extensive operations or in the treatment of ulcerations of the lower extremities which show no tendency to spontaneous healing. The transplantation of skin to such granulating areas as a means of covering them with epithelium has been employed for many centuries, but we owe to Reverdin and Thiersch the practical methods which we now employ. Reverdin (1869) used thin shavings from the epidermis including the papillary projections. These fragments were small, measuring not over 2 to 6 mm. in diameter. They were placed upon the granulating surface and fastened in position by strips of plaster. Twenty-four to thirty-six hours later these fragments were firmly adherent to the surface of the granulations, and after forty-eight hours began to show the pale bluish border characteristic of epithelial growth.

Thiersch (1886) modified this procedure in that he employed long strips of epidermis including a portion of the cutis. These strips can be of any convenient size, depending upon the technical skill of the operator and the available surface from which such ribbons of epidermis can be removed. An attempt is usually made to obtain fragments 10 to 12 cm. in length and 2 to 3 cm. in width. Thiersch also recommended the removal of the granulation layer with the curette and placing the grafts directly upon the normal tissues underlying the granulations. The results obtained by this method are very satisfactory, as large areas can be covered with epidermis in a few days. The same phenomena of growth are to be observed as previously described in the Reverdin form of grafting. While it is preferable to use skin obtained from the individual upon whom the grafting is to be executed, chiefly on account of the danger of the transmission of syphilis, it is possible to use grafts from other healthy persons or even skin from a freshly amputated limb. If the grafts cannot be applied immediately they may be kept for a short time in physiologic sodium chlorid solution (0.85 per cent.) until they can be applied. It is possible to keep such grafts for twenty-four hours, and successful results can be obtained even with strips which have dried somewhat, according to Wentscher, though this author has withdrawn his original statement concerning the possibility of grafting with skin which has been dried for two or three weeks. It is certain that some of the epithelial cells of the Thiersch skin graft retain their viability for three or four days if the strip be kept moist and not soaked in salt solution; but it is preferable in all cases to apply the graft as quickly as possible.

An interesting feature of the results obtained by skin grafting was early observed by Reverdin, that is, that if the skin of a negro is grafted onto the tissues of a white person the pigment gradually disappears from the grafted area and it remains permanently white. If white skin be transferred to a negro, pigmentation gradually takes place. This seems to be due to the fact that the pigment-bearing cells, the so-called chromatophores, wander out of the negro skin when it is transferred to a white person, and that in the white skin transplanted to a negro such pigment cells, which are present in small numbers even in the white skin, collect in greater quantities, or are transferred from the neighboring dark areas.

The microscopic details of the healing of the transplanted skin graft are relatively simple. There is an exudation of fibrin between the graft and the tissue upon which it is placed which fixes the epithelial layer firmly. Exudation of leukocytes and red cells takes place into the graft from this fibrinous layer, while vessels rapidly penetrate any portion of the corium which may have been transferred. No changes are seen in the epithelium for two or three days. Usually the upper layers macerate and can be removed by a gentle stream of water, leaving a clear, transparent, bluish-red layer composed of the cells of the basal region of the epithelium. After four days have elapsed very marked evidences of proliferation can be found in the epithelial cells. The connective tissue of the transplanted corium and of the subjacent tissues proliferates, forming a fresh granulation layer. In seven to ten days the grafted area is covered with thin though tender epithelium. Occasionally small projections of granulation tissue may be seen where the graft has not taken hold or where a portion of the wound has not been completely covered with skin. These areas, however, are rapidly covered by lateral growth from the neighboring epithelial borders. At the end of three or four months the papillary structure of the newly formed skin begins to be well marked. Elastic fibers are abundant, though usually smaller than those present in the normal skin. It is probable that they develop from the old fibers preëxisting in the deeper tissues in the neighborhood of the graft. After some time nerve fibers grow into the newly formed corium, which regains tactile sensibility first, then pain and temperature sense. Complete restoration often requires several years. The scar tissue beneath the epithelium continues to grow for some months.

Transplantation of Skin and Corium.—It is also possible to transplant large portions of skin, including a considerable part of the corium. Usually such transplantations are made with a pedicle to sustain nutrition of the part. Occasionally this is impossible. Such grafts are not, as a rule, as successful as the Thiersch grafts, owing to the risks of infection and the large amount of tissue which is left without blood-supply. The changes which take place are practically the same as those in the Thiersch grafts. The superficial epithelium dies; there is a necrosis of a considerable portion of the cells of the corium; granulation tissue forms between the corium and the surface upon which the graft is placed. The vessels from this tissue penetrate the grafted skin, which is thus gradually united to the tissues beneath it. Sensibility begins to return in about two months, but the normal tactile sense is not usually present for some years.

Healing of Tissues after X-ray and Radium Burns.*—After prolonged exposure of the skin to the action of the X-rays, especially from a low vacuum tube, or to powerful radium salts, a reddening or pigmentation of the surface is frequently noticed, beginning a few days after the exposure. About ten days after a prolonged exposure the reddening may increase and the skin may become necrotic. Large blebs containing blood are occasionally formed and sometimes a necrotic area in the form of a dry slough. Moderate exposures usually cause only a falling of the hair of the part treated, due to the atrophy of the hair-follicle.

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*While the necroses induced by the action of the X-rays and the radiations from radium are usually designated clinically as burns, there is some difference between these injuries and true burns incited by hot substances. The use of the word burn in this connection, however, is quite general, and it has been thought advisable to retain it here.

The stage of the injury which shows only reddening or pigmentation of the skin or destruction of the hair usually heals without treatment. Microscopic sections of such tissues show only slight evidences of degeneration of the superficial epithelium with a pigmentation of the deeper layers and a moderate exudative inflammation in the corium. Surfaces which have been burned more deeply show marked degenerative changes in the connective tissue, the fibers of which are often swollen, faintly staining, or altered into a clear, gelatinous mass taking a deep blue stain with hematoxylin. The surface epithelium becomes necrotic (Fig. 95) and may be raised by a collection of blood or serum under it in the form of a small bulla. The individual epithelial cells stain imperfectly, the nuclei not being differentiated from the rest of the cells. The slough which separates is composed of leukocytes, bacteria, and degenerated cells. In the connective tissue are many leukocytes and large flat cells of the type of plasma cells. The leukocytes and plasma cells frequently give rise to a copious infiltration of the perivascular tissues. The endothelium of the vessels is swollen, and in a large number of cases a marked endarteritis is present, especially when the burn has existed for a considerable time. In chronic burns a general thickening of all the coats of the vessel is produced.

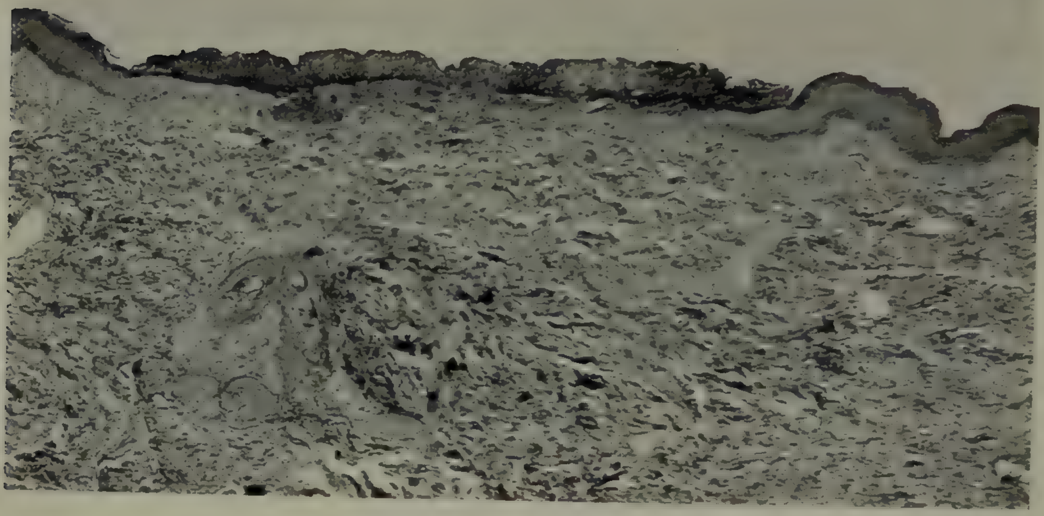

Fig. 95.—Radium Burn of Skin.
Showing the necrosis of the epithelium with the formation of a dry slough. (Photograph. Magnified 100 diameters.)

The granulation tissue of a fully formed ulcer due to X-ray or radium is marked clinically by its sluggishness and anatomically by the moderate number of vessels which it contains. These ulcers heal very slowly, often requiring one or two years of treatment before complete cure is obtained. Grafting with Thiersch skin grafts is not generally successful, but some observers have reported that the use of thick flap grafts resulted in prompt healing. The first phenomenon observed is that the granulation tissue underneath these thick grafts becomes much more vascular than before and that the tissue takes on a more healthy appearance. It has occasionally been observed that after the sloughing of such a flap the underlying granulations are sufficiently healthy to enable a Thiersch graft to grow satisfactorily.

Healing after Gangrene.—After interference with the proper circulation of an extremity or after the action of strong chemicals, such as carbolic acid (Plate IX), death of a considerable proportion of the injured tissue may take place. This necrosis is designated clinically as gangrene. The gangrenous changes may assume two forms, either the tissues dry up and remain uninfected or they may remain moist and then undergo putrefaction. The moist gangrene is more apt to be progressive than the dry, and the death of the patient often occurs by extension of the process which may result in a general infection before any reparative procedures make their appearance.

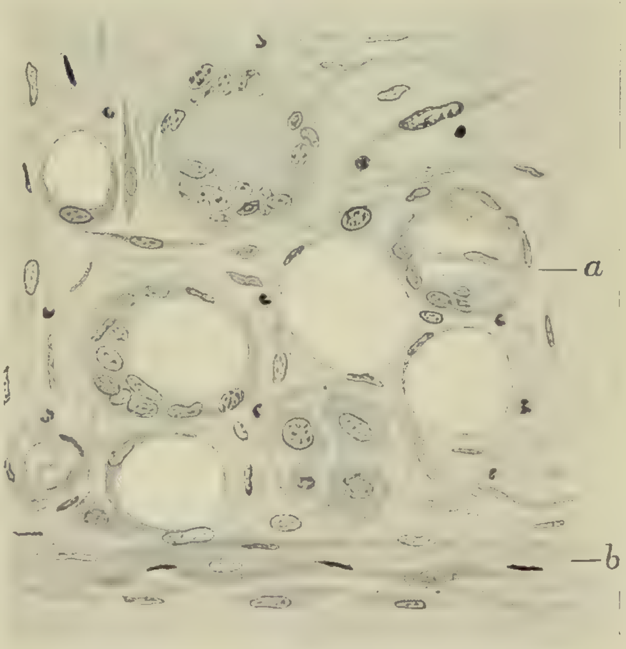

Fig. 96.—Regenerating Fat Tissue from a Case of Gangrene.

The clear spaces in the drawing represent areas in the cells from which the fat has been dissolved by the action of the hardening fluid.

In many cases of gangrene reparative processes begin as soon as the extension of the tissue necrosis has ceased. A so-called line of demarcation is thus produced between healthy granulation tissue on one side and dead tissue on the other. Small areas of gangrene such as are seen after the application of concentrated solutions of carbolic acid remain aseptic and dry, and in the course of a few days the dead tissues may be separated from the healthy, and at the line of separation the epithelium may be found to have completely covered the wound surface. The process is therefore similar to so-called healing under a scab and consists in the formation of a very small amount of granulation tissue, the absorption of small fragments of necrotic tissue which may remain on the surface of the wound, and, finally, the reparative hyperplasia of the surface epithelium growing in from the edges. Where the gangrene has involved a considerable portion of the limb the separation of the necrotic tissue from the healthy may be very slow and a very considerable production of granulation tissue may occur. It is then usually necessary to resort to operative procedures to obtain a cure. The method generally employed is to amputate through the healthy tissue above the line of separation, but occasionally a spontaneous cure is seen, the only operation necessary being the sawing of the bone to permit of the removal of the gangrenous extremity. Healing then takes place as described in the section on healing by second intention, the granulations being gradually covered by epithelium, preferably aided by the use of Thiersch skin grafts.

The Absorption of Blood-clots and Exudates and the Healing about Foreign Bodies.—The absorption of an inflammatory exudate in tissues may take place in two ways: (1) By a preliminary digestion of the solid particles which renders them soluble in the body fluids, the resultant fluid products being then carried off in the blood- or lymph-stream; (2) by phagocytosis, by which process the particles are inclosed in wandering cells, where they may be either digested or removed to some other tissue, such as the spleen or lymph nodes, where they are deposited. One of the most familiar examples of the solution of exudates is that shown in the fibrinous exudate of granulation or inflamed tissue, where the leukocytes are often surrounded by clear areas due to the solution of the fibrin by the cell ferments. An example of the mechanical removal of particles is the phagocytosis of the red blood-corpuscles or their pigment which occurs in the neighborhood of a subcutaneous injury with hemorrhage. In this case the blood-pigment may remain for a long time in the tissues unaltered but inclosed in the phagocytic cells, or it may be destroyed by a digestive process, or the pigment may be deposited in the spleen by the death of the cells inclosing the remnant of the coloring-matter.

The source of the ferments which act on dead cells as in the case first considered may be either inside or outside of the cell. It is undoubted that the leukocytes furnish a digestive ferment which may act on surrounding dead tissues (Fr. Müller, Opie), while it has also recently been shown that many body-cells are capable of self-digestion or autolysis. Such power of self-digestion may be demonstrated by preserving organs or inflamed tissues in toluol at incubator temperatures. Under these circumstances liver tissue, for example, will soften and its proteids will break down into bodies of the amino-acid group under the action of a proteolytic ferment, while under similar conditions the exudate in a pneumonic lung will occasionally become quite fluid. The phagocytic process may also remove bacteria from the tissues and the organisms often undergo destruction in the body of the cell, probably by the action of proteolytic ferments. Foreign substances in the tissues which are not soluble but are of small dimensions are usually removed through the nearest lymph-channel after being taken up by a cell. A good example of this procedure is the transfer of inhaled particles of carbon from the lungs to the bronchial lymph nodes.

Larger masses of foreign substances, which cannot be carried off by the phagocytic leukocytes, are usually inclosed in a new growth of connective tissue. In some way as yet not understood such foreign bodies stimulate the growth of cells. The form assumed by such cells is often that of a large mass inclosing all or a portion of the foreign body. This cell mass usually has numerous nuclei, and is known as a foreign-body giant cell. Such cells are often found in the tissues, closely arranged about either natural products, such as cholesterin crystals (Fig. 97), or sutures (Fig. 98), or fragments of bone broken off during the course of a fracture, or small foreign bodies accidentally introduced into healing wounds. Among the latter are sponge tissue, cotton fibers from dressings and pads, starch and lycopodium powders, and hair. The giant cells resemble in their morphology those incited by the poisons of syphilis and tuberculosis, and possess considerable power of locomotion, enabling them to surround the foreign particle.

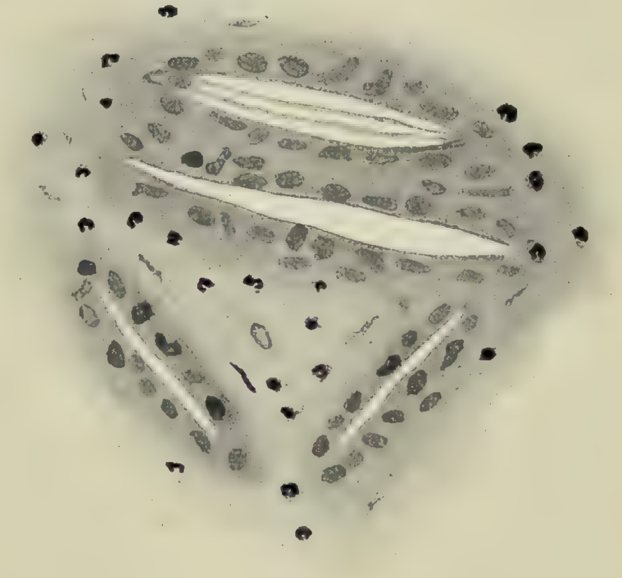

FIG. 97.—FOREIGN-BODY GIANT CELLS FROM THE WALL OF A CHRONIC ABSCESS OF THE BREAST.

The substance giving rise to these cells is cholesterin, the crystals of which fill the white spaces in the drawing.

A certain amount of tissue digestion and absorption may go on in the parts in contact with these cells. This absorption may perhaps best be seen in bone fragments which are being absorbed by the so-called osteoclasts or in the absorption and digestion of fragments of muscle in crushed wounds or of catgut sutures. Foreign-body giant cells are formed probably either by the junction of several individual cells or by progressive nuclear division without corresponding division of the protoplasm. There are reasons to believe that the nucleus may divide either directly or indirectly. Endothelial and connective-tissue cells probably furnish the individuals which undergo fusion.

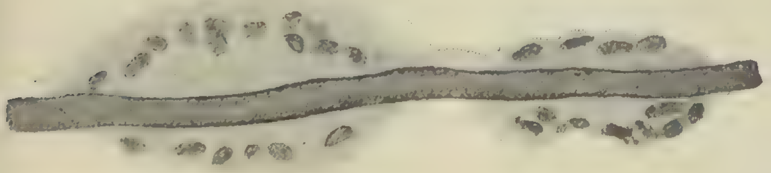

FIG. 98.—TWO FOREIGN-BODY GIANT CELLS FORMING ABOUT A SILK FIBER.

In addition to the giant cells there is usually formed about a foreign body of considerable size a layer of granulation tissue, the production of which, as previously mentioned, is apparently induced by the irritation of the foreign substance. This granulation tissue gradually becomes less cellular, the giant cells disappear, and finally the foreign body is inclosed in a thick capsule of fibrous tissue. Metallic substances, such as projectiles, plates to close trephine openings in the skull, or silver sutures, may be incased in fibrous tissue and remain for a long period without giving further disturbance. There is, however, a considerable difference in action between the different metals. Mercury, copper, and brass are apt to give rise to a progressive local inflammation which necessitates the removal of the substance. Iron and lead are often oxidized or eroded by the action of the tissue juices, but do not, as a rule, incite inflammation. Magnesium is rapidly dissolved with the liberation of gas. Silver seems to exert a distinctly anti-inflammatory and anti-bacterial action, while gold and platinum may be encapsulated without disturbance. There are a number of cases on record in which metal instruments left in the abdominal cavity at operation have been recovered at a second operation several years later in an unchanged condition except for the oxidation which has taken place, though occasionally the pressure which they exert on the mesentery or intestine in virtue of their weight when the patient stands upright may lead to sloughing of the bowel.

The injection of paraffin of either high or low melting-points into the tissues incites an inflammatory reaction. The soft paraffin is removed from the tissues fairly rapidly by the action of phagocytes and the breaking up of the mass by the ingrowth of connective-tissue cells. Paraffin of a melting-point above 55° C. is less rapidly invaded by the new connective-tissue cells and may remain encysted for a long period, though occasionally the foreign body excites an active inflammation which necessitates the removal of the paraffin. The morphology of the tissue about such a foreign body does not differ from that already described. It is composed of granulation tissue containing leukocytes and giant cells. Later, as the process becomes chronic, a firm scar tissue may be produced.

Catgut sutures introduced into the tissues give rise to an inflammatory reaction accompanied by maceration of the gut and infiltration by leukocytes. A catgut which has not been treated with strong disinfecting substances or has been sterilized by heat is more readily absorbed than catgut which has been impregnated, for example, with chromic acid, iodin, or oil. Catgut which has been sterilized by any of these agents usually incites a very considerable reaction with the formation of foreign-body giant cells. The method of absorption is, however, the same in all cases, partially by phagocytosis, partially by the solvent action of the ferments of the tissues.

HEALING IN NONVASCULAR TISSUES.

Repair in Cartilage.—As would be expected from the nonvascular nature of cartilage, the repair of the tissues takes place very slowly and imperfectly. Aseptic incised wounds in articular cartilage, made with a sharp instrument so that no serious destruction of tissue takes place, may heal, at least in young persons, by simple fusion of the wound-edges during the course of the growth of the cartilage, without evidences of inflammation or the production of granulation tissue. The cartilage cells do not show any evidence of unusual proliferation during the healing. The process consumes a very considerable time, even four to six weeks (Lefas).

Large wounds or ruptures in which there is considerable loss of substance are repaired by the production of soft connective tissue from the perichondrium, a process which begins about three weeks after the injury. Occasionally, evidence of proliferation of the cartilage cells can be noted with the formation of projections from the edges of the wound into the granulation tissue already produced in the incision by the ingrowth of germinal tissue from the perichondrium (Matsuoka). Small islands of cartilage are also occasionally found in the connective-tissue scar. This germinal tissue is then slowly transformed into cartilage, though the metaplasia may be very incomplete if the wound is large (Fig. 99). The healing is completed in from ten to twelve weeks. Fractures of bone of such a nature that the joint cartilage is included in the injury heal but slowly. Thiersch found no evidence of healing six weeks after an incision into the cartilage of a joint.

The scar tissue produced during healing not infrequently becomes partially or completely ossified, especially after fractures of the costal or thyroid cartilages (Paget).

Repair of the Cornea.—Superficial wounds of the cornea penetrating only the anterior epithelial layers are of special interest because they permit the study of epithelial regeneration without the confusion resulting from complicating phenomena which are present when the epithelium is injured over a very vascular tissue such as the corium. As the cornea contains no vessels there is no hemorrhage at the point of injury. A few hours after removal of a small amount of epithelium from the surface of the cornea, the neighboring epithelial cells wander by their ameboid activity over the surface of the injury, so that in about twenty-four, or at most forty-eight, hours the corneal connective tissue exposed by a small wound is completely covered with epithelial cells (Fig. 100). Within about eight to twelve hours after the injury, mitotic division of the nuclei of the epithelial cells begins. At about the end of forty-eight hours this proliferation is very active. It begins in the cells bordering the wound, but later, mitoses can be found in the epithelial cells which have wandered over the surface of the connective-tissue lamellæ and also at a considerable distance from the wound.

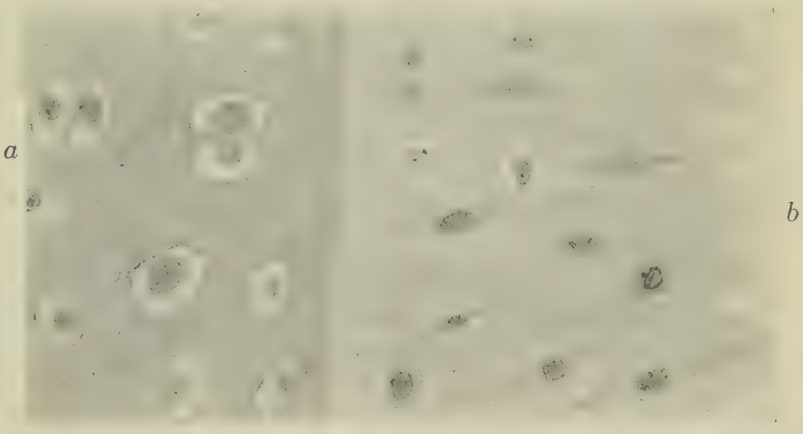

Fig. 99.—Section showing the Transformation of Fibrous Tissue into a Substance Resembling Cartilage during the Course of Healing of a Wound in Cartilage from a Rabbit's Ear.
a, New-formed cartilage; *b*, fibrous tissue which has filled wound.

Deeper injuries which separate the fibers of the connective tissue of the cornea heal more slowly. An exudate arises from the tissue spaces of the cornea which coagulates and fills the wound with fibrin. If the anterior chamber has been penetrated the aqueous humor also contributes a delicate coagulum to the mass occluding the wound. In twenty-four hours the fibrinous union is sufficiently dense to prevent the escape of fluid even when considerable pressure is exerted on the eyeball. The connective-tissue fibers of the cornea gradually become opaque and swollen, probably

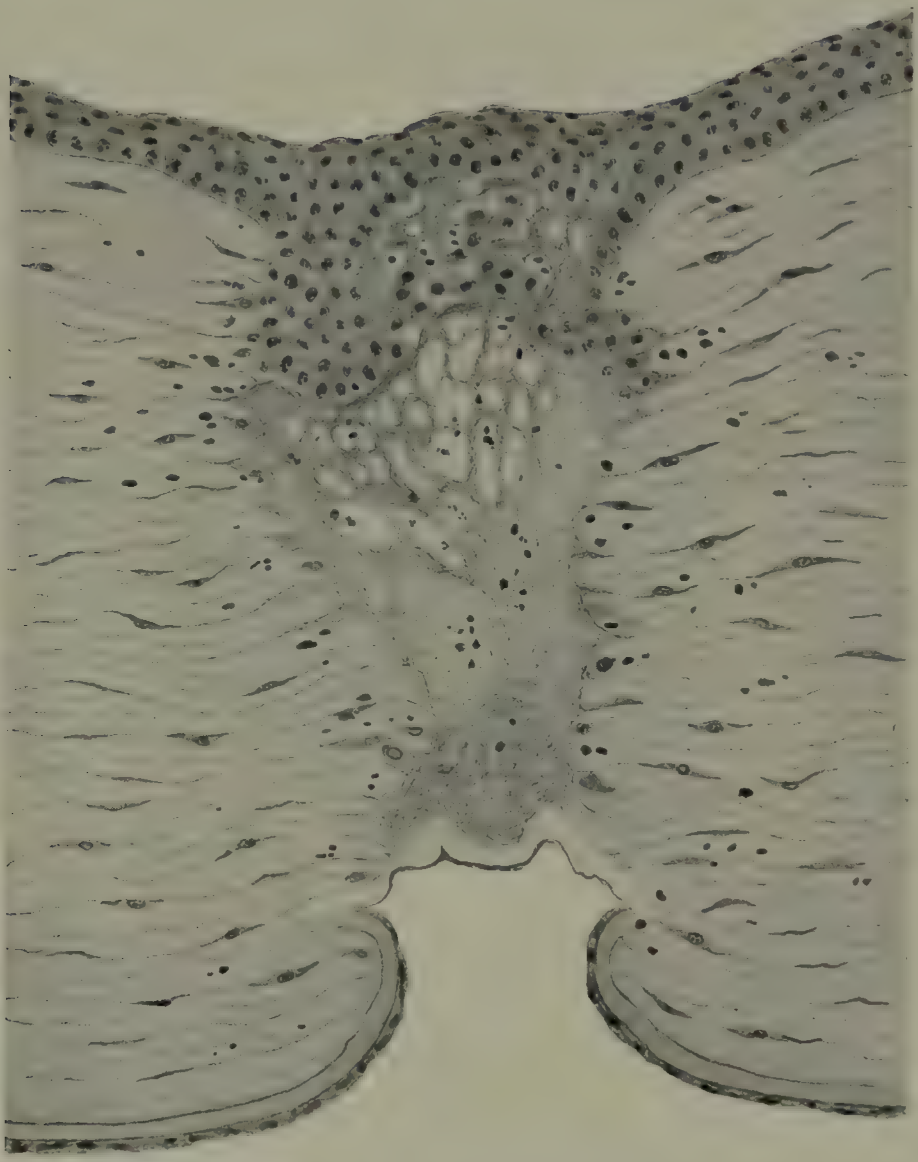

Fig. 100.—Repair of Penetrating Corneal Wound by Fibrin and Leukocytes. The epithelium has extended over the anterior surface. (After Ranvier.)

from the action of the fluid from the anterior chamber. The nuclei of the corneal cells enlarge and the bodies send out projections through the tissue spaces toward the wound. The epithelial layer on the anterior surface folds down into the wound following the contraction of the anterior elastic layer. In two or three days the plug of epithelium fills the anterior portion of the wound (Fig. 101). Many polynuclear leukocytes are present in the edges of the wound and in the fibrinous exudate. The epithelial cells and the connective tissue soon show evidence of proliferation and a small wound is rapidly filled up with fibroblasts. These cells are covered in three to four days on both the anterior and posterior surfaces by a fresh layer of epithelium, while the connective tissue gradually becomes firmer and ultimately leaves a translucent or opaque scar at the site of the trauma, the amount of opacity depending on the quantity of connective tissue formed in the healing. At the end of a week the superficial epithelium and Descemet's membrane are completely regenerated. A few leukocytes are present in the cicatrix. In fourteen days healing is practically completed. The nuclei of the fibroblasts become smaller and stain more deeply; the formation of connective-tissue fibrillæ can be noted; while most of the leukocytes have disappeared.

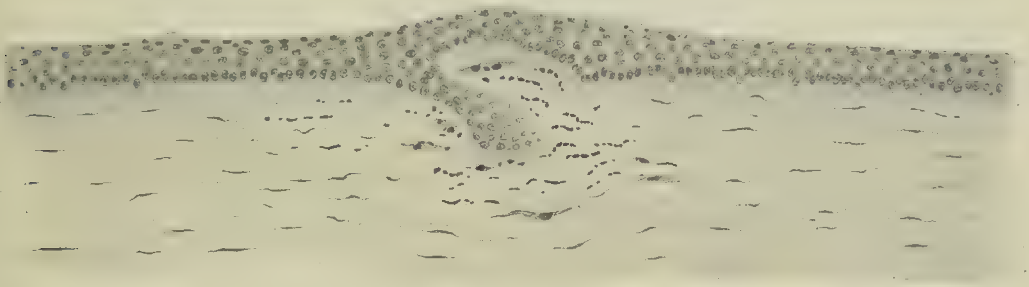

FIG. 101.—SUPERFICIAL WOUND OF A RABBIT'S CORNEA AFTER TWENTY-FOUR HOURS. Proliferation of the corneal tissue is beginning.

If an active infection of the wound occurs the repair of the cornea is complicated by the exudation which collects in the anterior chamber (hypopyon) owing to the chemotactic action of the toxins of the bacteria. The granulation tissue in the wound contains large numbers of leukocytes which have emigrated from the episcleral vessels or from the conjunctiva. Numerous small vessels are present which have grown in from the sclerotic. The iris not infrequently adheres to the posterior corneal surface, the union being produced by fibrinous adhesions. The scar produced is usually much larger and more opaque than in wounds uniting primarily.

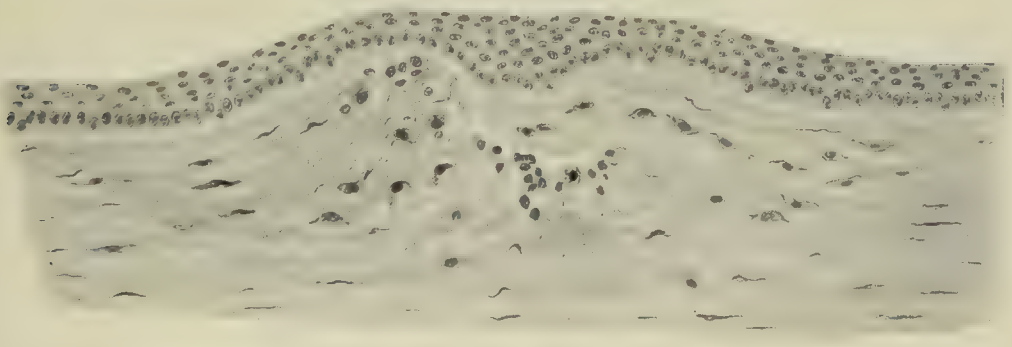

FIG. 102.—SUPERFICIAL WOUND IN A RABBIT'S CORNEA AFTER SEVENTY-TWO HOURS. The corneal connective tissue has filled the wound.

Transplantation of Corneal Tissue.—In cases of leukoma of the cornea following a perforation of that tissue attempts have been made to implant a fresh transparent portion of cornea removed from an animal. Fuchs reported in 1894 that thirty cases of transplantation of the cornea in man had resulted in only two fairly successful operations. At first the transplanted fragment becomes very cloudy, then vessels penetrate from the sclera, and though some clearing of the cornea takes place with reduction of the vascularity, yet results are not very good. Usually the vision is not much better than ability to count the fingers at a distance of three or four feet. In animals the results have been somewhat better, and here the details of the process have been more thoroughly traced. In a certain number of cases the transplantation resulted in complete restoration of tissue, the inserted fragment retaining perfect transparency. Excessive thickening of the anterior and posterior epithelial layers may occasionally remain. The chief cause of failure is the formation of granulation tissue and the penetration of numerous vessels into the substance of the cornea.

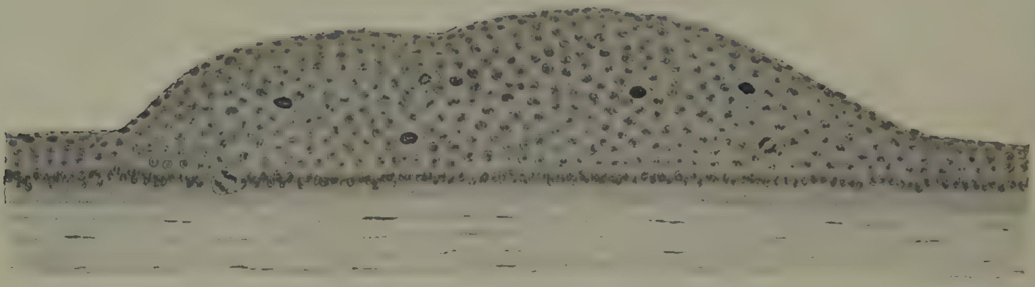

Fig. 103.—Rabbit's Cornea Eight Days after Injury.
Excessive growth of the epithelium covering the site of the wound.

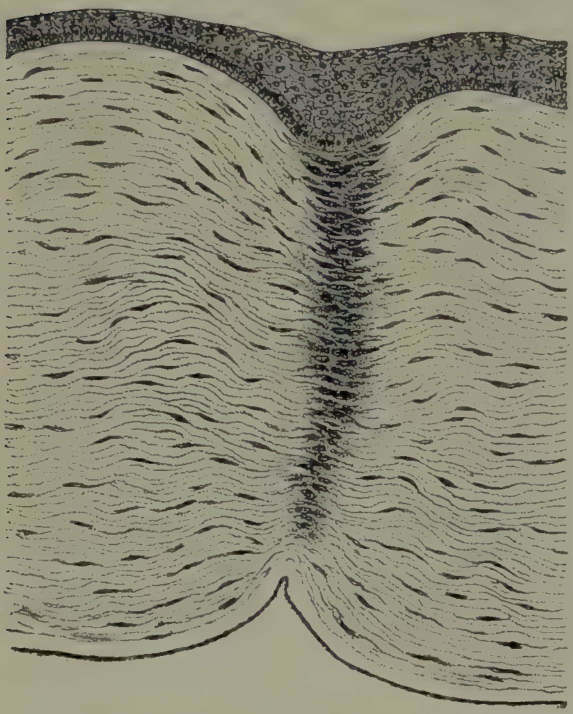

Fig. 104.—Healed Wound in Rabbit's Cornea. Two Weeks after Injury.

A slight opacity is noted on examining the cornea, due to the connective-tissue cells seen in the line of the scar.

Repair of the Sclera.—Wounds of the sclera heal in a somewhat different manner from those of the cornea, the new fibers which form a permanent union between the separated parts being derived largely from the episcleral tissue and the choroid. The closure of the wound takes place primarily by the formation of fibrin which begins to be replaced at the end of two days by granulation tissue. From the second day on, slight changes can be noted in the sclera, the cells of this layer proliferating and adding to the granulation tissue already formed.

REPAIR IN MUSCULAR TISSUE.

Striated Muscle.—After small portions of muscular tissue have been destroyed, for example, by a gunshot or stab wound, a very complete regeneration of the injured muscle may take place, so that no trace of the injury can be made out even with the aid of the microscope. Aseptic incisions through muscles often heal very completely, the injured fibers regenerating, while the small amount of connective tissue which is formed gradually retracts and appears so like one of the normal trabeculæ between the fibers that it is impossible to distinguish it from one.

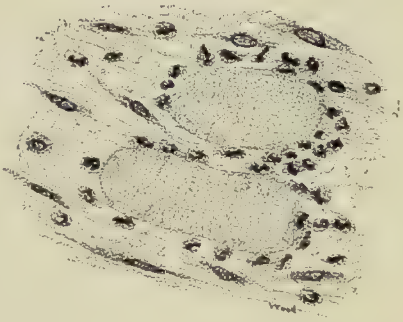

Fig. 105.—Degenerated Muscle Fibers in a Laparotomy Wound being Absorbed by Phagocytes.

When a large amount of muscular tissue is crushed, or when the muscle is torn or cut and the separated ends retract so as to leave a considerable space, the healing is very imperfect anatomically, though the functional result may be good. The muscle fibers retract into their sheaths and assume a homogeneous appearance, losing all evidences of striation. Later, larger or smaller, oval or cylindric fragments of necrotic muscle fibers form which are usually absorbed in a short time (Fig. 105). Granulation tissue is produced at the site of the injury and at the same time the healthy muscle tissue close to the wound begins to proliferate, the nuclei multiplying by mitosis and the cell-body losing all striation and becoming granular (Fig. 106). The result of this proliferation is the formation either of knob-like ends to the fiber, of a forked fiber, or of free rounded muscle cells. The last may often be seen surrounded by the granulation tissue, and probably die and are promptly absorbed. The end result of the healing process in an extensive wound of muscle is the formation of a scar of dense connective tissue in the substance of the muscle. A few tapering, slender muscle fibers extend for a short distance into the scar, but they form only a small number of those originally proliferating, and are functionally unimportant. The scar may later shorten and give rise to annoying contractures, as is occasionally seen after tearing the sternomastoid muscle during delivery. The muscle may very rarely

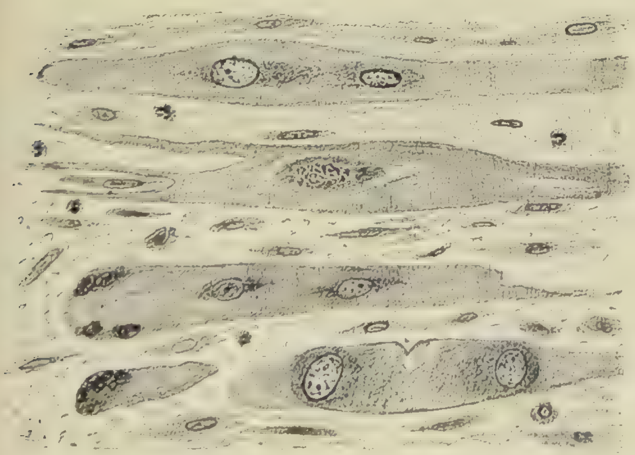

Fig. 106.—Reparative Changes in Heart Muscle. The branching of the fibers and the formation of knob-like ends are well shown.

become ossified, giving rise to a hard tumor composed of more or less imperfect bone surrounding atrophied muscle fibers.

Wounds of the heart-muscle heal by the formation of new connective tissue, although some evidences of reaction may be seen in the muscle cells. The imperfect mitoses which appear occur only temporarily in the muscle cells soon after the injury and the amount of new muscle formed is quite unimportant in the healing process.

Unstriated Muscle.—The regenerative powers of smooth muscular fibers are very slight. Mitoses are seen in the muscle fibers after incision into the uterus, bladder, or gastro-intestinal tract, but the healing is almost entirely accomplished by connective tissue and not by newly formed muscular fibers.

REPAIR IN TENDONS.

The repair of tendons after tenotomy or suture is quite perfect both anatomically and functionally, and it is also possible to obtain perfect anatomic union in grafting one tendon upon another. After avulsion of a tendon from its muscular connection, however, the union is usually less satisfactory, as the large amount of scar tissue formed is likely to interfere with the function of the muscle.

As a tendon is practically a non-vascular fibrous tissue, the vessels being very few and small, the phenomena attendant upon its healing are relatively simple and resemble those seen in the cornea under similar circumstances.

In the repair of severed tendons two factors must be considered: one, the regeneration due to the proliferation of the elements of the tendon itself, the other, a new growth of cells from the peritendinous connective-tissue sheath. The space between the separated ends of the tendon is promptly filled with a fibrinous network containing red and white blood-cells. Soon after the injury the polynuclear leukocytes begin to appear in the tissues and are very abundant at the end of forty-eight hours. The cells of the tendon proliferate late, the first mitoses appearing at the third or fourth day after the injury, while proliferation of the connective-tissue cells of the sheath is active on the second day. The formation of a blood-clot between the separated ends retards rather than aids healing. A sort of cellular callus is formed of granulation tissue which unites the separated ends and, gradually undergoing progressive changes with which we are familiar from the previous pages, forms a dense connective-tissue scar uniting the two ends. Slight differences can be detected between the proliferating connective-tissue cells and the true tendon cells.

The scar tissue in due course of time contracts and becomes so dense that it can be distinguished from the normal tendon only by slight differences in color and in structure, such as the greater vascularity of the scar tissue, the large number of nuclei, and the irregularity of the connective-tissue bundles, the fibers of the normal tendon having a strikingly even texture.

Resorption of the surplus tissue formed by the hyperplasia of the synovial sheaths takes place, as a rule, leaving the tendon free in its sheath even though an abundant hemorrhage or a mild infection has occurred. Occasionally, however, dense adhesions are left between the sheath and the synovial covering of the tendon, which may result in serious functional disturbances. If the tendon be sutured with silk or other non-absorbable material, foreign-body giant cells form about the thread. Such cells are probably due to the fusion of connective-tissue cells.

The time required for healing is from two to ten weeks, depending upon the form and extent of the implantation or plastic operation employed and whether infection has occurred or not. The healing of tendons is much delayed by infection, as a moderately extensive necrosis of the adjacent parts is not infrequent in consequence of bacterial invasion.

REPAIR OF BONE.

In injury to bones caused either by transverse or by longitudinal stresses producing fractures or fissuring of the bony tissue, or in perforating wounds produced by bullets or sharp instruments, the damage is rarely confined to the bony structures alone. The periosteum is usually torn across or raised from the shaft of the bone by a separation of the fragments, and the connective, muscular, and vascular tissues immediately surrounding the site of the injury are damaged. Only in fissures or simple fractures without displacement of the fragments are the injuries to the surrounding tissues kept within moderate bounds. Blood exudes into the structures about the point of the fracture, the amount varying a good deal, depending upon the density of the tissue which surrounds the injured part. If a vessel of considerable size be injured, the extravasation of blood may be very considerable and the fluid is apt to infiltrate between the tissues and appear under the epidermis even at a considerable distance from the point of fracture. Usually, however, the amount of blood which escapes is slight and chiefly confined to the medullary cavity, while the discoloration of the skin is due to the bruising received during the accident. In compound fractures the destruction of tissues and the amount of blood set free are naturally much greater.

A short time after the fracture is produced reparative changes commence about the site of the injury, which may result in a complete restoration of the structures, so that after a few months scarcely a trace of the injury may be apparent.

The healing or union of fractures is accomplished not by growth of bone cells but by the production and organization of new connective tissue which surrounds the fragments and is derived chiefly from the periosteal membranes of the bone. The reparative process may be considered in two stages; first, that which completes the union of the parts, in other words, the formation of a callus; second, that in which the redundant portions of the callus are absorbed and the ossification is completed by the deposition of lime in the newly formed tissue. Strictly speaking, however, both of these processes in some degree go on simultaneously. The absorption of small fragments or bone splinters begins a short time after the injury, and calcium salts are deposited in the newly formed osteoid and cartilaginous tissue within a week or ten days after the occurrence of the fracture. The callus which unites the bones is produced, as previously stated, by a growth of cells chiefly from the periosteum of the bone. The inner, more vascular layers of the periosteum are the chief source of this cell growth, though the outer layer of the periosteum occasionally takes part in the process. A proliferation of cells of the marrow also contributes to the formation of the callus. This so-called internal periosteum or endosteum produces the same sort of structures as the periosteum. The callus produced from the periosteum is often called the periosteal callus; that from the inner surface of the bone, the myelogenous callus, while the new tissue which lies between the ends of the fragments is commonly designated the intermediary callus. The intermediary callus is almost entirely produced by the growth from the periosteum penetrating between the fragments. In early childhood the cartilage which exists at the epiphyseal junction is capable of forming a callus.

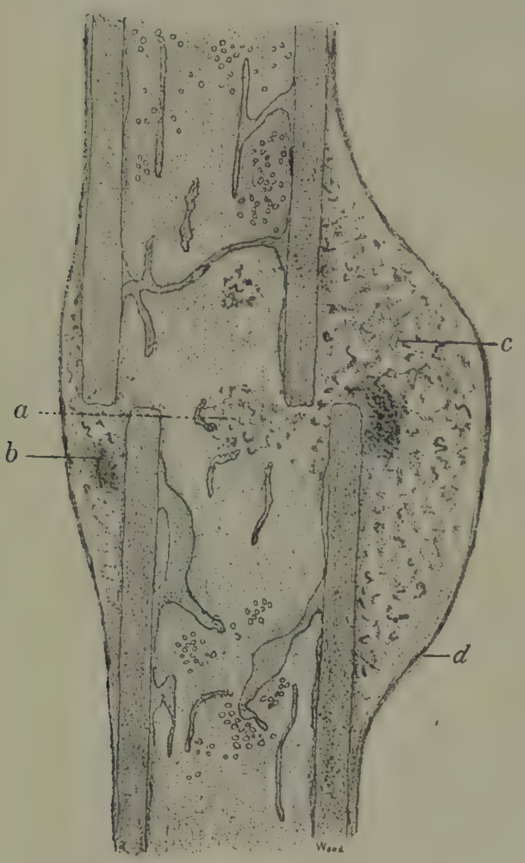

Fig. 107.—Fracture of Rib.

Specimen obtained ten days after injury. The formation of a periosteal callus is well advanced. *a*, Osteoid tissue in the medulla of the bone; *b*, cartilage; *c*, osteoid tissue from periosteum; *d*, periosteum stretched by new growth of osteoid tissue.

The amount of callus produced is very variable and depends partly upon the condition of the bone at the place of fracture and also upon the size of the bone and the form of the injury. A very large callus is formed in fractures of the shafts of the long bones, and a much smaller growth is usually seen in connection with fractures at the epiphyseal end of the long bones, in fractures of the bodies of the vertebræ, and the flat bones of the pelvis and skull. In fact, the external callus produced in the fractures of the cranial bones can scarcely be demonstrated by palpation. When the displacement of the fragments is considerable a very large callus is the rule, unless such displacement is so great as entirely to prevent bony union. In this condition the bones may be united by fibrous tissue only, a final ossification not taking place.

Details of the Healing.—The first evidence of the inflammatory reaction in the periosteum is a softening and swelling of this tissue. Leukocytes emigrate from the vessels, the endothelium of which is markedly swollen. At the end of forty-eight hours proliferation of the connective-tissue cells begins. The soft tissue thus produced by the inner layers of the periosteum consists at first merely of a very vascular connective tissue, containing numerous spindle or irregularly shaped cells or osteoblasts, which lie in a stroma which is partly hyaline and partly fibrous tissue. About four or five days after the occurrence of the fracture a change takes place in the fibrous tissue which results in the formation of small masses or clumps of a substance resembling bone but not containing calcium salts (Fig. 108). This "osteoid" tissue, as it is called, is ultimately changed into bone, any excess being finally removed by the osteoclasts. The connective tissue in the interstices becomes altered to a marrow-like substance. The hyaline areas referred to above develop into the so-called chondroid tissue or into true cartilage. While the amount of cartilage which is formed in fractures in which there is but little dislocation of the parts is less than when marked deformity is present, yet it has been shown (Ziegler) that even under most favorable apposition moderate amounts of cartilage are produced during the course of callus growth, and this cartilaginous part of the callus is considered to be of great importance in the construction of the final bone which cements the fragments. The larger portion of the cartilage is produced by the inner layer of the periosteum. The final ossification takes place by direct transformation to bone after the cartilage has become fully vascularized. Osteoblasts, according to Ziegler, play a subordinate part in the process and appear only in the later stages of healing (Fig. 109).

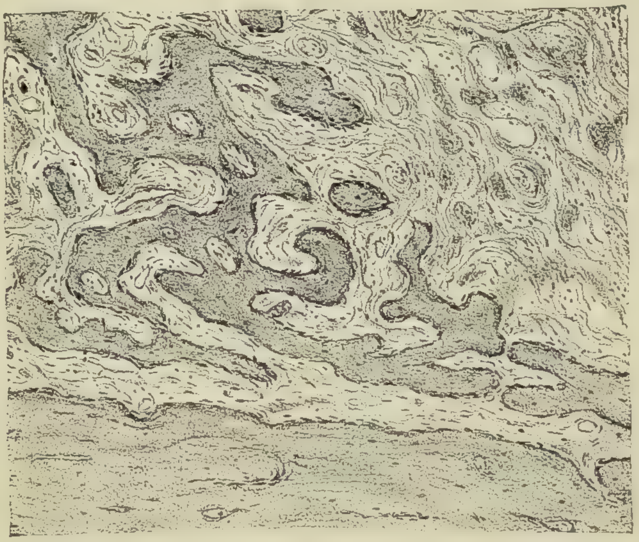
FIG. 108.—OSTEOID TISSUE.

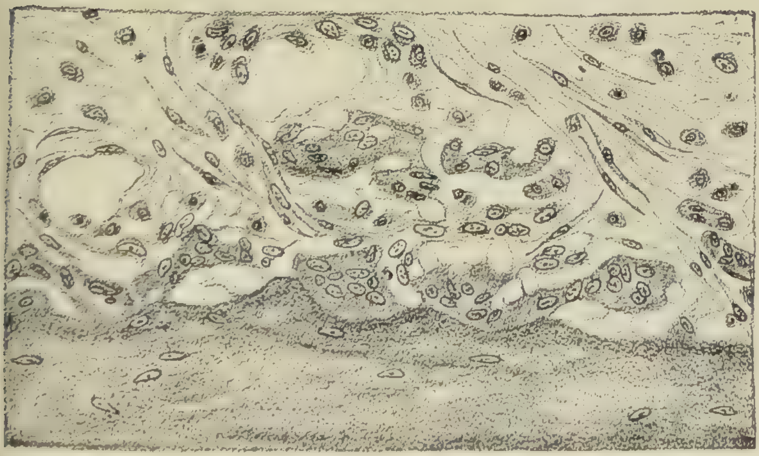
FIG. 109.—OSTEOBLASTS ABSORBING DENSE BONE. TWO WEEKS' CALLUS.

When the ends of a fractured bone are separated by too great an interval to permit of suitable callus formation, or if muscles or tendons are forced between the ends or if proper immobilization of the fragments has not been obtained, either union may not take place at all or the bones may be united by a dense fibrous band. Under these circumstances the removal of foreign substances and the proper coaptation of the fragments, after freshening the ends, will usually result in union. Compound fractures heal in a manner similar to those in which no complicating wound exists, but if infection occurs, union may be delayed or very imperfect. The suppuration is likely to incite thromboses of the vessels in the neighborhood and death of the periosteum with necrosis of the bone as a result. The abundant granulation tissue formed is also apt to interfere with proper callus formation.

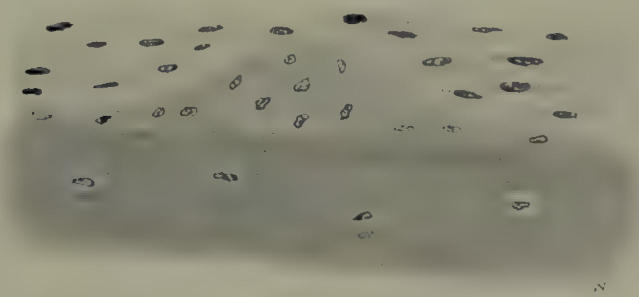
FIG. 110.—GROWTH OF NEW BONE DIRECTLY FROM OLD WITHOUT INTERMEDIARY STAGE OF THE FORMATION OF OSTEOID TISSUE.

The callus as finally produced is usually more abundant than is necessary for the proper union of the bone ends. Several weeks after repair is begun and considerable ossification of the callus has occurred, the trabeculæ of the redundant external and internal callus begin to be absorbed. This absorption is executed, it is generally believed, by large multinuclear cells known as osteoclasts, which in some manner erode the bone, possibly by the formation of lactic acid or a ferment. Some observers are inclined to regard the osteoclasts as of minor importance in the resorption and consider the regressive changes in the callus as of the type of a disease atrophy, or possibly as a resorption due to the general ferments of the tissues. The result of this absorption is that the bone is practically restored to its original condition, the medullary cavity becoming patulous and only a slight thick-

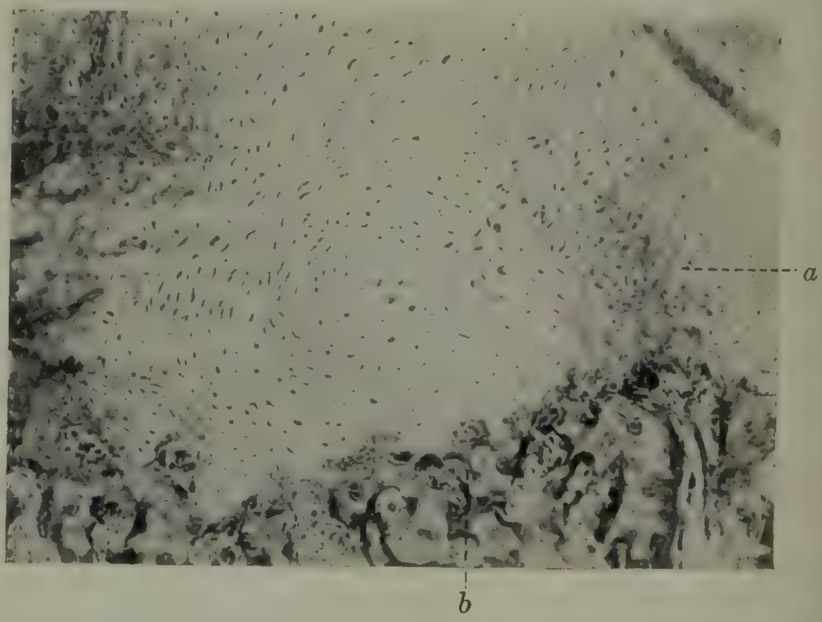

FIG. 111.—NEWLY FORMED CARTILAGE AND OSTEOID TISSUE FROM FRACTURE OF A RABBIT'S FEMUR, SEVEN DAYS AFTER INJURY.
At *a* ossification of the cartilage is beginning. At *b* slight calcification has taken place in the trabeculæ of the osteoid tissue.

ening being apparent on the outer aspect of the shaft. The fibrous portion of this redundant callus is also reduced in volume by gradual contraction of its elements and shrinkage of its blood-supply.

The closing of cavities in bone has been referred to under the heading of Healing under a Blood-clot. Where the injury is aseptic, as in a trephine wound of the skull, the button of bone is occasionally replaced in the cavity and allowed to heal *in situ.* The replaced bone is gradually absorbed, while at the same time osteoid tissue is produced from the borders of the wound and grows through the soft tissue left after the removal of the lime salts. In these cases the replaced bone acts only as a support for fresh tissue, just as in healing under a blood-clot. If the bone is not returned to the cavity, the space fills with blood, which is gradually replaced by granulation tissue, and a fibrous scar is ultimately produced.

REPAIR AFTER INJURY TO BLOOD-VESSELS.

The healing of wounds in blood-vessels differs somewhat from the process as observed in other tissues, because of the absence of capillaries from the inner and median layers of the vessel and from the fact that a blood-current at considerable pressure is in contact with the intima at the wound surface. A large tear or incision into a large vessel or a complete transverse incision rarely closes spontaneously, because the fibrin which forms from the action of the cellular ferments on the blood is quickly washed away by the current. Injuries to capillaries or small vessels may be promptly closed by blood-plates and fibrin, and later, when inflammatory proliferation of the cells of the vascular walls takes place, a complete restoration may occur.

Small Puncture Wounds of the Wall of a Blood-vessel.—A small puncture wound of a vessel, such as may be produced, for example, by accidental pricking with a suture needle, is closed by deposition of blood-plates and fibrin on and about the injured area. Leukocytes and red cells are later entangled in the fibrinous mass and the resulting thrombus may occlude the vessel or may remain as a parietal growth which is gradually altered into connective tissue by replacement with fibrous elements derived from the endothelium (Baumgarten) or, what is more probable, from the cells of the media and adventitia. Later an abundant growth of elastic tissue takes place from the intimal layer (Marchand). The usual course of the healing is that the thrombus shrinks and forms a sclerotic patch in the wall and does not wholly occlude the lumen of the vessel. If the blood-pressure rises after the stage of shock has passed the fresh clot may be dislodged (secondary hemorrhage) or a cavity may be produced containing fluid blood which is ultimately confined by a growth of connective tissue, thus forming a traumatic aneurism. Such a condition is not infrequently seen after gunshot wounds of vessels.

Wounds Completely Severing the Vessel.—When a large artery is severed the hemorrhage which results is usually fatal unless artificially checked. Exceptionally, however, in loose tissues the ends of the vessel may retract and the elasticity of the walls cause a narrowing of the lumen to such an extent that the blood-stream is slowed and thrombus formation is possible. In dense structures the resistance offered by the tissues to the extravasation of large quantities of blood may confine the hemorrhage to narrow limits and the clot which rapidly forms checks the bleeding. In soft organs or hard tissues, such as liver or bone, or when the artery is thickened by disease, retraction is not always possible, and severe and occasionally uncontrollable hemorrhage is likely to result from a vascular wound. This condition necessitates the use of special hemostatic methods in wounds of these parts, as, for example, the application of the cautery, steam or hot water in wounds of the liver, or of wax in plugging bleeding vessels in bone. If, however, the injury to the vessel is due to crushing or tearing of the tissues, the edges of the inner layers of the vessel may curl up inside the lumen and partly close it, so that a thrombus rapidly forms in each end of the separated tube. A similar thrombus caps the end of the vessel and assists in checking the flow of blood. The further changes are replacement of the fibrinous deposit with connective tissue derived from the median and outer layers of the vessel, and partly, according to some observers, by the metaplasia of the endothelium into connective tissue.

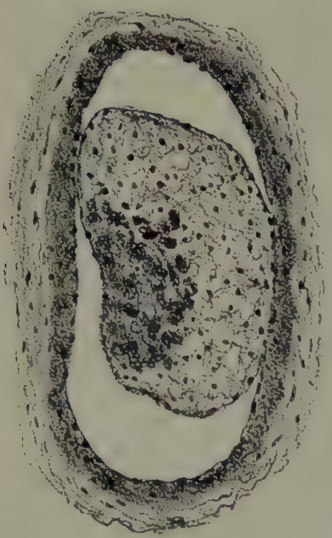

FIG. 112.—ORGANIZATION OF A THROMBUS AFTER SLIGHT INJURY OF A VEIN.

The thrombus has been covered by endothelial cells and is composed of a network of fibrin infiltrated with leukocytes and endothelial cells, a portion of the fibrin still remaining as a granular mass.

Healing after Ligation of Vessels.—When a vessel is ligated or clamped, the pressure causes rupture of the intima and then of the elastic layer. These structures retract, curl up in the lumen, and are promptly covered by a fibrinous thrombus deposited from the blood-current. Usually this thrombus does not extend far along the course of the vessel, but is chiefly confined to an area close to the ligature. The lining endothelium rapidly extends over the thrombus (Fig. 112) and its organization takes place in a few days, leaving a sclerotic patch in the wall. Where the vessel is diseased or where the circulation is poor a large thrombus may form, occupying a considerable extent of the vessel. When two ligatures are applied to the vessel a short distance apart, the blood in the lumen remains fluid and thrombi are formed only at the contracted areas where the endothelium is injured, though occasionally in old persons with arteriosclerosis or in marantic people a complete thrombus of the vessel may be noted. Ligatures applied to vessels with septic endarteritis or endophlebitis are apt to excite more or less extensive thrombosis. Such extensive thrombi are apt to be a source of great danger to the patient, for extension to the next collateral vessel not infrequently takes place with the production of septic emboli and wide distribution of the inciting agents of the disease.

Thrombosed vessels heal in the same manner as those which are cut across, that is, the thrombus is replaced by connective tissue with complete obliteration of the lumen. Occasionally, however, even in septic thrombi the canalization of the thrombus takes place, with more or less perfect restoration of the lumen.

The microscopic details of the healing process in blood-vessels may be summarized as follows: When a vessel is compressed or gently ligated so that a slight injury is produced to the endothelial layers without at all destroying the other coats, fibrin and blood-plates are deposited within five to ten minutes even if restoration of the blood-current has taken place. If the media and adventitia are penetrated this thrombus extends through the incision into the tissues (Eberth). Within a short time mitoses appear in the endothelium near the injured area, and these cells rapidly proliferate and cover the injured area. Later the connective-tissue elements of the media and the adventitia proliferate, forming granulation tissue which replaces the thrombus with the ultimate development of a firm connective-tissue layer closing the injury. New elastic fibers are produced in the intima and media. The muscular fibers seem to play little or no part in the healing process. The amount of vascularization of the scar tissue depends upon the extent of the lesion. With extensive injuries numerous capillaries are formed by budding from the vasa vasorum about two weeks after the injury, and ultimately the restoration of the wall is quite perfect.

REGENERATION AND HEALING IN LYMPH NODES.

Regeneration of lymph nodes may take place after the excision of these organs. Such reproduction has been seen after complete removal of the axillary nodes for carcinoma of the breast. The new formed nodes may be reproduced from fragments of preëxisting nodes or from fatty tissue. The numerous collections of lymphoid cells normally present in the subcutaneous fat probably act as centers for such regeneration. A similar development of a special type of lymph-node, the so-called hemolymph node, has also been observed.

The wound produced by excising a portion of a node heals by a new formation of connective tissue arising chiefly from the capsule, but partly from the fibrous trabeculæ of the perinodular tissue, and also the cells of the node reticulum.

REPAIR OF THE CENTRAL NERVOUS SYSTEM.

A regeneration of the nervous tissues of the brain or spinal cord after injury does not take place to any considerable extent. In a study of wounds of the brain by Hegler, Chenzinski, and others, no evidence of increase of the brain cells or fibers could be demonstrated during the course of the repair. The trauma usually incites extensive necrosis and softening of the brain tissue. An inflammatory reaction takes place at the periphery of the broken-down tissue. A slight hyperplasia of the glia has been noted, but healing takes place after absorption of the softened brain substance, chiefly through an increase in the connective tissue.

If infection of the wound takes place the destruction of brain tissue may be very extensive and a so-called hernia cerebri result. The protruded mass is not, however, composed of brain tissue but of granulation tissue, often containing necrotic nerve fibers or cells.

In animal experiments in which brain tissue was destroyed either by excision of a portion of the cortex or by puncture wounds with a hot needle, mitotic division in the nuclei of nerve-cells and other evidences of an attempt at repair have been observed near the injured area. But as the studies of Coën, Sanarelli, and Tschistowitsch have also shown that while shortly after an operation in animals or after wounds of the brain in man, mitoses and other evidences of growth can be noted, not only in the special connective-tissue framework of the brain, but in the nerve-cells themselves, yet ten to twelve days after the operative procedure the mitoses cease to be demonstrable, the nerve-cells apparently undergo destruction, and there is a moderate growth of glia cells with final closure of the scar by granulation tissue derived from the connective tissue of the vessels.

The same lack of regenerative power is noted in connection with accidental injuries to the cord in man and following experimental destruction of portions of that structure in animals. No extensive functional or anatomic regeneration of the tissue takes place, though after compression or destruction of the cord an occasional growth of fine nerve fibers occurs in the anterior and posterior portions of the cord, these fibers being derived from the gray substance of the anterior horns. The newly formed fibers first appear along the small vessels at the periphery of the gray substance, then pass along the central vein to the sulcus longitudinalis anterior. On the distal side of the compressed area a similar group of nerve fibers has been demonstrated. Such attempts at repair of the cord, however, do not give rise to complete functional restoration of the tissue, and are apparently only the result of the response of the nerve fibers of the pyramidal and lateral columns to growth stimuli, such as may be noted after section of the peripheral nerve. Fibers have been demonstrated growing from the posterior roots after injury of the latter, the direction of the filaments being centripetal.

Partial functional restoration (Stewart) has been observed in a few cases of complete transverse lesion of the cord after prompt union of the separated ends by suture, and is probably due to such fiber regeneration as described above.

Gross defects in the cord, as in the brain, are healed by a connective-tissue hyperplasia filling the spaces.

Whether after slight, aseptic injuries of the brain involving only a small number of fibers or cells there can be a regeneration of the injured tissues or not is as yet undecided. The most recent study on the subject is that of Borst, who, working with young animals, found that there was no new formation of permanent nerve-cells, but did find that a very considerable new growth of medullated fibers took place into the injured area which had previously been filled by hyperplasia of the glia cells.

DEGENERATION AND REGENERATION OF PERIPHERAL NERVES.

From the time when Cruikshank made the first observations on the regeneration of nerves, the problem as to the conditions and methods of nerve healing has always occupied a prominent place in surgical pathology. The importance of such regeneration was not only recognized in connection with the degeneration and loss of function after severing of nerves in incised wounds or inclusion of trunks in a bony callus after fracture; but it was emphasized by the unfortunate paralyses which occurred in the practice of the early surgeons, who, from lack of accurate anatomic knowledge, occasionally included the main nerve-trunks in the ligatures intended for vessels alone.

Advantage is now frequently taken of the regenerative capacity of the nerves to restore the function of the part rendered anesthetic or paralyzed. By suitably freshening the severed ends and suturing them together a partial or even complete repair with functional restoration may be accomplished. From another point of view, however, the regenerative capacities of resected nerves may occasionally be undesirable, as after resection of the Gasserian ganglion for trigeminal neuralgia, when the neuralgia may again appear after the reunion of the newly formed nerve fibers (Garrè).

The microscopic phenomena observed after division of a peripheral nerve were first reported by Nasse, who describes the breaking up of the primitive nerve fibers and the appearance later of the myelin droplets.

In 1850 Waller discovered the facts from which he formulated the well-known law bearing his name, that the nerve fibers degenerate after separation from their trophic centers. These centers lie in the cells of the anterior horn of the spinal cord for motor nerves and in the spinal ganglia for the sensory nerves. According to Waller, the peripheral end of the divided motor nerves degenerates completely, including the axis-cylinder and the sheath. These observations were subjected to much criticism, and shortly after this time it was even claimed that a nerve could be cut and then reunited by a suture without any anatomic degeneration taking place; in other words, that primary union of the nerve was possible. Later experiments have shown that this is not true, and that complete peripheral degeneration with loss of function takes place after section of motor nerves, accompained by a centripetal atrophy extending over a space comprised by several nodes of Ranvier, and that there are accompanying alterations in the central ganglionic cells whose peripheral fibers have been injured.

The changes in the sensory nerves after section are in general the same, but differ in their direction. If, for example, the sensory bundles are cut between the cord and the spinal ganglia a centripetal degeneration occurs extending far up in the cord and also a short distance downward, involving the posterior column. If cut peripherally to the ganglion the degeneration takes place throughout the length of the fibers and involves even the terminal organs such as the motor end-plates in the muscles or the so-called tactile bodies.

Compression of a nerve-trunk in a callus or tight bandage or by invasion of the nerve by the cells of a new growth does not always induce degeneration in all the fibers. Even after prolonged pressure a few fibers in the nerve bundle may remain uninjured.

Degeneration of Nerves.—There is still much uncertainty concerning the exact details of the degenerative and regenerative process, but according to our present knowledge the changes which take place are as follows:

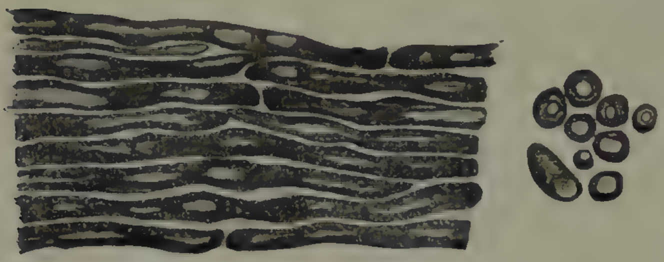

Fig. 113.—Normal Nerve Fibers.
Longitudinal and transverse sections made after treatment with osmic acid.

The first microscopic alterations noted after the section of a nerve are swelling of the medullary tubes at the cut end. The contents of the neurilemma is altered to a homogeneous, darkly staining mass. The axis-cylinders are thickened by the formation of little bead-like masses along the fiber, while the myelin flows from the cut sheaths. These changes seem largely due to the effect of the injury and have been designated traumatic degeneration. If the nerve has been compressed instead of cut, the medullary sheath and the axis-cylinder are pressed aside so that only the empty sheath of Schwann remains to connect the two filaments. In twenty-four hours or later, depending upon the species of animal used in the experiment, the phenomena due to central and peripheral degeneration of the nerve make their appearance. These consist in an irregular breaking up of the myelin, an edematous infiltration of the nerve fibers with serous fluid, and an irregular swelling of the axis-cylinder which later breaks up into granules. The elements of the nerve show evidences of degeneration close to the point of injury but not at any distance along its course. This early degeneration usually does not extend in either direction much beyond the first node of Ranvier, though it occasionally may go to the second node from the injury.

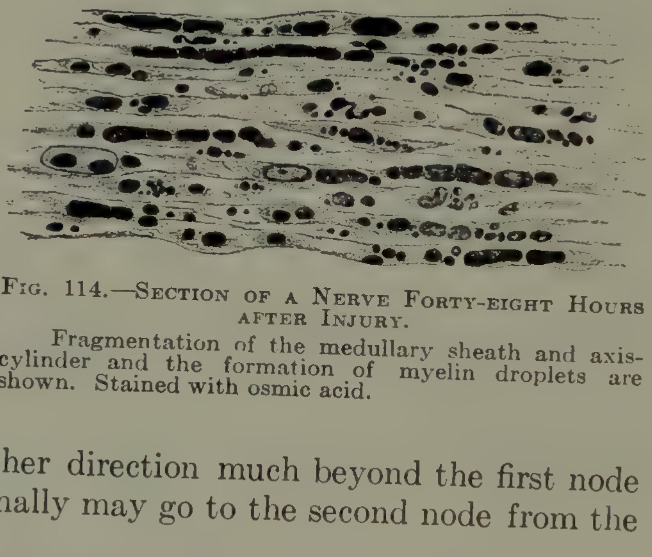

Fig. 114.—Section of a Nerve Forty-eight Hours after Injury.
Fragmentation of the medullary sheath and axis-cylinder and the formation of myelin droplets are shown. Stained with osmic acid.

The second day after the transection of a nerve the medullary sheath breaks up into fragments which at least twenty-four or forty-eight hours later separate into smaller particles of oval form or occasionally as long cylinders with rounded ends. These fragments lie within the remains of the sheath of Schwann. At about the same time the axis-cylinder shows alterations in its staining reactions and loss of function. Degeneration of the fibers soon takes place, the fragments often assuming a spiral or wavy outline, or they may break up into smaller fibers, or appear irregularly swollen. These secondary fibers are often embedded in the fragments of the myelin and may, with the latter, entirely disappear. The degeneration takes place more rapidly in sensory than in motor fibers.

Regeneration of Nerves.—An active proliferation of the cells of Schwann's sheath begins while the degenerative changes are still progressing. The nuclei of the sheath enlarge; their chromatin becomes more evident; while the cells occupy the space between the myelin drops and may act as phagocytes for the removal of these drops or the remnants of the axis-cylinder. The leukocytes which have collected about the site of the injury fulfil a similar function.

The result of this proliferation, according to most observers, is merely a regeneration of the sheath of Schwann. Some, however, are inclined to believe that the nerve fibrils which are ultimately produced in a degenerated nerve-trunk are derived from the proliferated cells of the sheath. If the first assumption is true, then the axis-cylinder must grow out from the central ganglion cell or from an undegenerated fiber extending from it. This means that such a fiber is projected through a number of inches or even feet in the course of its growth. For example, it is not uncommon to see the musculospiral nerve regenerate quite perfectly after being freed from compression in the callus of a fracture or united after traumatic separation of the nerve-trunk. In this case the fine axis-cylinder fibers must have grown along the atrophied nerve bundles for a distance of at least a foot and a half to two feet. This method of projection of the axis-cylinder from a ganglion cell is that observed embryologically in the course of development of the peripheral nervous system, and there are many physiologic reasons for believing that this type of regeneration takes place.

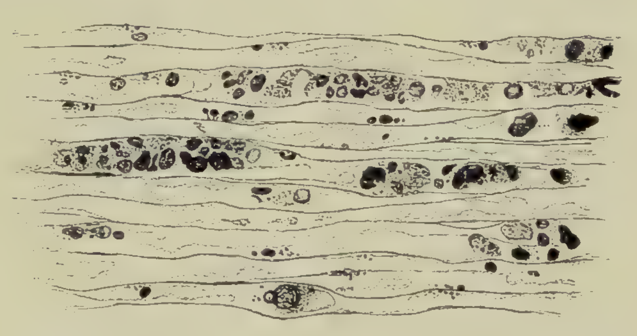

FIG. 115.—SECTION OF A NERVE THREE WEEKS AFTER INJURY.

The cut shows partial absorption of the remains of the medullary sheath and the myelin droplets. Stained with osmic acid.

A smaller number of authors, among them Marchand, Ballance and Stewart, and Bethe, think that to a certain extent the regeneration is discontinuous and that the different segments of the sheath form short nerve fibers which eventually anastomose to produce a continuous axis-cylinder.

However this may be, the regeneration of the severed axis-cylinders commences from the central nerve-trunk in a few days after the injury. The central end of the old axis-cylinders swell and give off a number of much finer fibers which extend out through the remnants of the sheath of Schwann into the granulation tissue which forms at the site of the section of the nerve. This is filled in a short time with numerous fibers projecting from the central end of the nerve. These newly formed fibers are often spirally arranged or wrapped about each other. They may grow in connection with remnants of old fibers, and if the peripheral end of the nerve is not more distant than 2.5 cm., they may enter the old sheath of Schwann to form a series of small bundles, five or six being contained in the space previously occupied by a single axis-cylinder. A very delicate medullary sheath surrounds each of them, which probably is formed at the same time as the axis-cylinder, and ultimately a new neurilemma is formed.

The reason for the entry of the newly growing fibers into the old nerve-trunk, and their ultimate union with the peripheral end-organs in the muscles, skin, and blood-vessels, is not yet understood. Forssman suggests that a stimulus of the same nature as that which gives rise to the chemotaxis of leukocytes attracts the nerve fibers to the old sheath. Perhaps the chemical products due to the destructive metabolism of the peripheral stump may have such an action. It has been shown experimentally that a regeneration takes place over a greater distance if the growth of the nerve fibers is directed by inclosing the cut ends within a small tube, such as a cylinder of decalcified bone or formalinized gelatin, or even by uniting the separated stumps by strands of catgut. In animals regeneration has been occasionally noted over a distance of 10 cm.; but 2.5 to 3 cm. is the limit of unaided regeneration in adult human beings, and good results are rarely possible unless the ends can be closely approximated. If the peripheral nerve has been removed by amputation of the part, or if it is at too great a distance for the regenerated fibers to bridge, the growth may form a mass of nerve tissue which caps the central stump and is known as an amputation neuroma. The time required for a complete restoration of physiologic function in a recently injured nerve is very considerable, usually at least three to four months.

Restoration of sensation is usually more rapid than restoration of motion, probably in consequence of an anastomotic ingrowth into the nerve-trunk, or the region supplied by it, of sensory fibers from other and uninjured tracts. The complete restoration of motion is dependent not only upon regeneration of the nerve-trunk, but upon the nutrition of the muscle whose nerve-supply has been cut off and upon the condition of the motor end-plates. Return of function after grafting is always slow, especially so when uniting nerves with different central ganglia, as is done, for instance, in facial palsy when the facial is united to the hypoglossal. Under these conditions the new center in the brain must be educated to produce coördinated impulses.

Changes in the Ganglion Cells after Injury of the Nerve Fibers.—According to the original view of Waller, degeneration of nerve fibers extends only in a direction away from the trophic ganglia. Some time after his investigations were published it was found that a long time after the section of a motor nerve under conditions in which no regeneration was possible, as, for instance, after amputation of a limb, the anterior horn of the spinal cord on the side on which the nerve was sectioned diminished in size and the number of ganglia cells in the anterior horn of that side was also diminished. This central degeneration of nerve fibers is much slower than the peripheral or Wallerian type, the latter requiring days, while the central degeneration, though beginning in about two weeks, takes months or years to reach its full development. There are also certain anatomic differences in the two forms, for example, the granules as demonstrated by the Marchi method are smaller and more widely separated than in the Wallerian form. The Nissl method of demonstrating the structure of nerve-cells also shows that a chromatolysis occurs in the ganglion cells within twenty-four to forty-eight hours after an injury of the nerve fiber. At first this breaking up of the chromatic substance takes place only in small areas of the cell, generally at the point of entry of the axis-cylinder. In a few days, however, the entire nerve-cell shows a diffuse fragmentation of the Nissl bodies. As the changes progress the nucleus assumes a position at the periphery of the cell and finally disappears, while the entire cell ultimately degenerates. Those cells which are not completely destroyed undergo a regeneration beginning about three weeks after the injury. The nucleus assumes a central position; the cell-body regains its normal form; and the chromatic substance is regenerated. This reparative process takes place whether there is regeneration of the nerve-trunk or not; but if the nerve is not regenerated a secondary, possibly disuse-atrophy takes place in the ganglion cells a number of months after the primary cell change, which ultimately results in a total destruction of the nerve-center, whose cells act as trophic agents for the nerve-trunk. Such degenerations are frequently noted in connection with amputations as stated above. If the nerve fiber is torn away from its ganglion, the degeneration of the ganglion cells is much more complete than that which follows a mere section of the nerve.

The degree of these retrograde changes and the number of cells which are destroyed have a fixed relationship to the length of the nerve. The nuclei in the medulla with short nerve-trunks show greater changes than those in the spinal cord, while the degenerations are more marked when the nerve is cut close to its origin than at the periphery. Final degeneration, however, does not destroy all the ganglion cells of a given nucleus, especially in sensory trunks, for cases of restoration of function have been noted after the nerve has been separated from its central cells for a very long period. Partial restoration is not infrequently seen after a nerve suture or graft when the parts have been separated for over ten years.

REPAIR AFTER WOUNDS OR INFLAMMATION OF SEROUS SURFACES.

Pleura, Pericardium, Peritoneum, Omentum.—Wounds of serous surfaces can be considered together, as the mode of healing differs only in unimportant details.

In uninfected, sharply defined wounds of any of these membranes healing is begun by the filling of the defect with fibrin and leukocytes or blood-clot. This is rapidly replaced by new connective tissue derived from the cells of the subserous layer, and the wound is finally covered by the surface epithelium. Occasionally this growth of the lining epithelium may be quite extensive and extend to some distance along a sinus, a phenomenon most frequently observed in a wound of the pleura following an operation for empyema. The reparative action of the epithelium takes place by two methods: in one the cells crawl over the injured surface in virtue of their power of ameboid motion; in the other there is mitotic proliferation of the epithelia near the denuded area and a repair of the denuded surface by multiplication of cells, precisely as has been described in the healing of wounds of the skin.

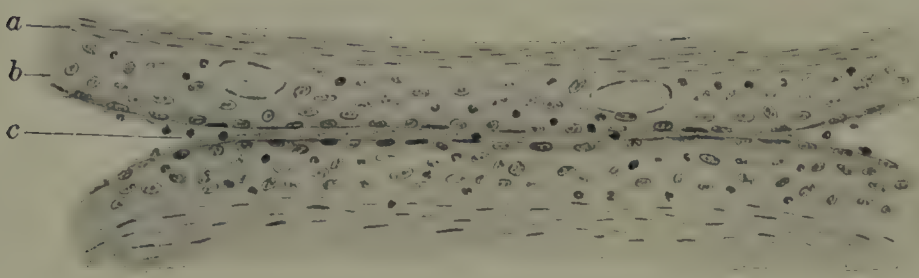

Fig. 116.—Adhesions Between Two Loops of Gut.
Early peritonitis following appendicitis: *a*, Muscular coat; *b*, serous layer; *c*, layer of fibrin.

It is generally believed at present that the epithelium lining the serous cavities retains its specific qualities, but some observers (Ranvier, Cornil, Graser, Borst) hold the view that a metaplasia of these cells into connective tissue occurs and that this assists in the formation of the granulation tissue produced during repair. Among the phenomena which have led to the latter belief is the rapid disappearance of the surface epithelium when two serous surfaces are approximated. Under these circumstances fibrinous adhesions form very rapidly and it is sometimes difficult or impossible to demonstrate the epithelial layer.

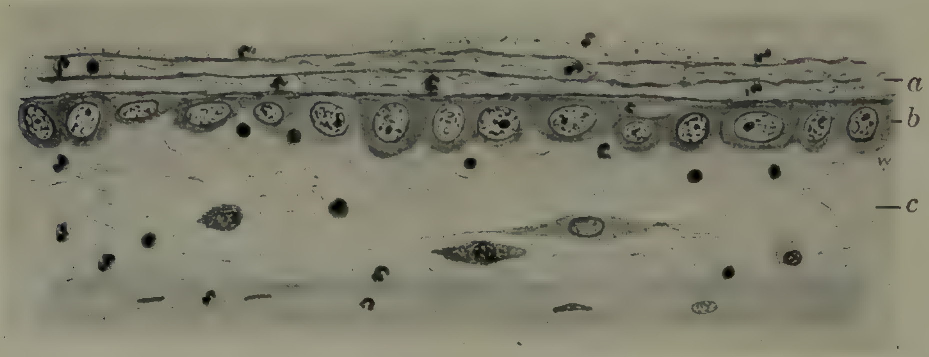

Fig. 117.—Early Peritonitis about Twenty-four Hours after Perforation of Typhoid Ulcer.
The flat cells covering the surface of the gut (at *b*) are swollen and covered with fibrin (*a*) and leukocytes. The subserosa (*c*) is edematous

From a clinical point of view the formation of adhesions between two apposed serous surfaces is of greater practical interest than the repair of wounds. Very slight injuries to the peritoneum, either mechanical or chemical, give rise to such adhesions, a fact frequently made evident during the course of a post-mortem examination of a subject upon whom laparotomy has recently been performed. Under these conditions the omentum and loops of gut are almost invariably adherent to the inner surface of the laparotomy scar, even when less than twenty-four hours have elapsed since the operative interference. The exudation of fibrin and adhesion of the contiguous surfaces is no doubt in many cases due to a terminal infection with bacteria from the skin of the abdomen transferred into the peritoneal cavity by the instruments, temporary packing, or the hands of the operator, but in many of the cases no bacteria can be demonstrated. If such adhesions are separated the serous surfaces will be noted to be duller than normal and hyperemic; and small subserous ecchymoses are apt to be present. These are especially noticeable in the omentum, which may even contain very considerable effusion. Microscopic examination shows that the epithelium is not infrequently present, though it may be swollen and irregular in shape. A layer of fibrin containing leukocytes unites the two surfaces (Fig. 116). The surface cells near the adhesion are swollen (Fig. 117). In a few days such adhesions become organized by the growth of the connective-tissue cells from the submucosa and the penetration of the granulation tissue so formed by blood-vessels. Such adhesions may be drawn out into long strands by the peristaltic action of the gut and are sheathed by proliferation of the neighboring epithelium. Many of the adhesions so formed become ultimately absorbed, as may be noted in persons in whom several laparotomies have been performed at a considerable interval.

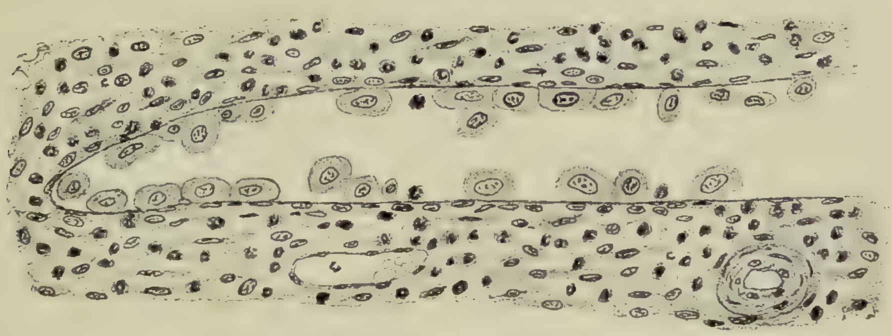

Fig. 118.—Acute Peritonitis from a Case of Appendicitis.
Showing the swelling of the peritoneal epithelium but without a fibrinous exudate.

REPAIR IN THE BRONCHI AND LUNGS.

Small puncture wounds of the lung may heal, when without further complications, by the formation of fibrinous adhesions between the edges of the severed pleura and the organization of the extravasated blood in the alveoli. The resulting scar may be small and not interfere with the function of the organ.

Large wounds, on account of the extreme vascularity of the lung tissues, are usually accompanied by extensive hemorrhage, the pleural cavity being more or less filled with blood while the lung collapses or the alveoli become filled with blood. In case death does not occur from hemorrhage, the clot which forms at the site of injury may be absorbed with the production of a large scar of connective tissue, the cells of the alveolar epithelium not taking an important part in the regenerative process. Occasionally wounds of the lung heal on the pleural surface, leaving a large cavity into which a bronchus may open.

If the wound of the thoracic wall is promptly closed the lung may expand in a short time and begin to fill the pleural cavity. If air is admitted, however, at the time of the injury, or if infectious substances enter the pleural cavity, an empyema is likely to result with the formation of extensive adhesions between the lung and the parietal pleura. Unless the pleural cavity is drained death is then likely to result from sepsis.

Abscesses of the lung have been successfully opened and drained, the granulation tissue of the abscess membrane extending and closing the defect; while after the inflammatory process has subsided and the lung has become adherent to the chest wall, the air in the pleural cavity may be gradually absorbed with the reproduction of the normal lung volume. Usually the portions of the lung not involved in the abscess become emphysematous and general adhesions remain permanently between the parietal and visceral pleural leaves.

Gunshot wounds of the lung, made by the modern, high-velocity, small-caliber, military bullets may heal without symptoms, wounds by such projectiles not usually being accompanied by infection. Large-caliber lead bullets generally cause death by hemorrhage from the lung tissue; but occasionally they have been found to penetrate the parenchyma of the organ and heal *in situ*, the foreign body being surrounded by dense connective tissue.

The microscopic details of repair in the lung tissue have been studied chiefly by Cornil and Marie. They found that a short time after injury of the lung an inflammatory reaction took place, not only involving the interstitial tissue, but giving rise to an exudate filling the alveoli in the neighborhood. The walls of the alveoli were thickened by the growth of connective-tissue cells and were infiltrated by leukocytes. The epithelium lining the alveoli became swollen, showed evidences of proliferation, and occasionally formed giant cells. In the course of ten days the exudate had become organized into connective tissue which later formed a dense cicatrix.

Wounds of the bronchi heal by the formation of a connective-tissue scar. The lining epithelium regenerates rapidly and covers the surface of the injured part. The cartilage shows but little reparative capacity.

REPAIR IN THE STOMACH AND INTESTINE.

The healing of perforating wounds of the stomach and the intestine is complicated by the fact that these organs usually contain a fluid with a rich bacterial flora, the exit of which through the wound sets up a peritonitis. Very small puncture wounds are occasionally spontaneously healed without the production of a local or a general peritonitis, by the early formation of adhesions between the surface of the wound and a neighboring fold of the omentum or intestine; but this is relatively rare. Whether healing takes place or not depends also upon the amount of food or fecal matter contained in the stomach and the intestine. Perforating wounds of an empty stomach may occasionally heal either without the production of a severe peritonitis or with a localized inflammation. Perforating intestinal wounds, however, are nearly always accompanied by more or less extensive acute suppurative inflammation.

The muscular coat of the stomach and intestine may contract over a small perforating wound and prevent the escape of the contents. This is occasionally seen after perforations with small-caliber bullets. The pouting of the mucous membrane may block a small wound and thus prevent leakage. Wounds in which the peritoneal surface is inverted are more apt to heal spontaneously than those in which there is a protrusion of the mucous membrane. This fact is taken advantage of in suturing incisions or injuries in the gastro-intestinal tract, the rapid union of the peritoneal surfaces being aided by purse-string or inverting sutures which bring the peritoneal surfaces in apposition and retain them in that position. If, on the other hand, the mucous coat or the submucous coat is apposed, union is delayed because of the necessity of the resorption of these tissues with the production of granulation tissue before union can be accomplished. The adhesion of the serous surfaces takes place very rapidly, loops of gut which have been in close contact for an hour often requiring some force to separate the apposed peritoneal layers. When so separated the surface is duller than normal and microscopic examination shows that there has been a slight exudation of fibrin over the surface. This fibrinous exudate becomes quite considerable in amount in a very few hours, and thirty-six to forty-eight hours after the apposition has been produced the union is quite firm. In about six days union is complete. At the same time the epithelial cells of the peritoneal surfaces swell; leukocytes emigrate from the capillaries and also enter the fibrinous layer from the peritoneal cavity if the inflammation is extensive (Fig. 116). In the neighborhood of such a union, especially if the infection is localized or the organisms not especially virulent, the epithelial cells of the peritoneal surface may assume a high oval or cylindrical form (Fig. 118). If, however, the infection is a rapidly spreading one, the peritoneal surface near the locality of the injury may be covered with a thick layer of fibrin infiltrated with leukocytes and red cells. The final result of the process is the production of a firm connective tissue which is penetrated by blood-vessels and forms a dense scar connecting the two surfaces. Under the influence of the peristaltic action of the intestine these adhesions may be stretched to a considerable extent or, if of small dimensions, may be finally absorbed. The surface of the scar is covered with a new growth of epithelium.

The muscular layer of the gut plays no part in the regenerative process, though occasionally mitotic figures may be found in the nuclei of the cells, but instead the injured muscle is replaced by a connective-tissue scar.

The mucous membrane of both intestine and stomach is capable of very extensive regeneration and even considerable surfaces may be denuded and yet perfect restoration result. The contraction of the muscular layers diminishes the size of the wound and the surface is promptly covered by a layer of cells of the flat epithelial type, while the glandular structures develop later; usually several months are required. Where the wound is very extensive and penetrates all the coats, as in ulcer of the stomach, the resulting cicatrix may cause a very considerable narrowing of the lumen of the organ (hour-glass stomach, local stenosis, etc.). A similar contraction of the connective tissue in the scar may produce stenosis of an anastomotic opening between portions of the gastro-intestinal tract.

REPAIR IN THE GALL-BLADDER.

Wounds of the gall-bladder heal quite rapidly by new growth of connective tissue and regeneration of the epithelium, the final result being the complete restoration of the epithelial lining. The process is complete in about ten days. The restoration of the lumen and the epithelium is occasionally observed after ligature of the common duct.

REPAIR IN THE URINARY BLADDER AND URETERS.

Wounds of the urinary bladder and the ureters heal by a fibrinous cementing of the apposing surfaces, with the production later of granulation tissue and the formation of a cicatrix. The muscular fibers play little or no part, while the epithelium regenerates very completely. Occasionally wounds of the bladder are spontaneously closed by fibrinous adhesions between the omentum and the peritoneal surface of the bladder. The fibrinous layer becomes organized and ultimately the bladder-wall itself unites. This protective action of the omentum has been occasionally applied in surgical practice to the repair of extensive injuries of the bladder or ureter.

REPAIR IN THE LIVER.

Evidences of regeneration of the liver cells are frequently noted after lesions of the organ which result in the destruction of large amounts of the parenchyma. Examples of such conditions are the hyperplastic areas seen in cirrhosis of the liver and the regeneration which takes place of the liver cells and especially of the bile-ducts in acute yellow atrophy.

In young animals one-half to three-fourths of the liver can be removed, and the organ ultimately be restored to its normal size in the course of two months by hypertrophy of the remaining tissue. Such extensive regeneration, however, is not possible in man, and the tissue in the partial reproduction which takes place is probably not functionally useful.

If the liver is incised or cauterized there is a necrosis of the cells due to the trauma, followed by exudation from the vessels, which forms a clot over or in the wound. In the course of forty-eight hours a more extensive necrosis of the tissue takes place owing to thrombosis of the capillaries, and, finally, a reaction zone is established at the limit of the necrosed area, at which point a large number of leukocytes collect. At this point many nuclear fragments and portions of cells are collected. Reparatory processes begin at the end of about forty-eight hours. The hepatic cells, the epithelium of the biliary ducts, and the interstitial connective-tissue cells all proliferate. The proliferation of the hepatic cells does not result in the production of permanent tissue, for they atrophy and are later absorbed, and the wound is closed ultimately by a connective-tissue scar containing a few bile-ducts.

REPAIR IN THE SPLEEN.

Wounds of the spleen are very apt to lead to rapidly fatal hemorrhage owing to the great vascularity of the organ, so that reparative results are only noticed in small tears due to external violence, to gunshot wounds with small-caliber bullets, and to stab wounds. If the organ is enlarged and congested as in typhoid fever small wounds of not more than 1 cm. in length, made by the puncture of a hypodermic needle, have been known to cause death. The extent of the wound is due to the fact that the spleen is moved downward by the diaphragm during the muscular fixation of the latter owing to the patient's effort to remain quiet despite the pain of the puncture. In animals, wounds or partial excisions of the organ have been repeatedly made to study the nature of repair. No regeneration of the splenic tissue has been observed, the wound healing in all cases by the new formation of connective tissue. Reported cases of total regeneration of the spleen have not been substantiated. Small tears in the human subject occasionally heal, first, by the coagulation of the blood in the fissure and on the surface of the spleen, and then by the organization of this clot by the growth

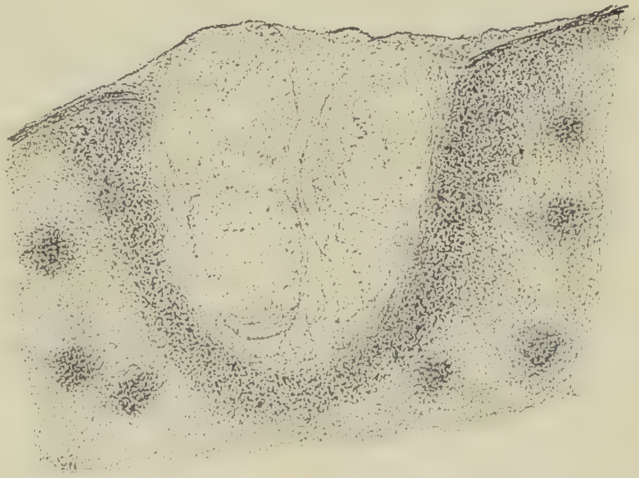

Fig. 119.—Tear in Spleen Eighteen Hours after Injury.

The wound has been closed by a blood-clot and there is an accumulation of leukocytes and necrotic cells about the periphery of connective tissue into it. Fig. 119 shows an eighteen-hour tear in the spleen with a beginning zone of reaction about the blood-clot, the patient having died from other injuries. Healed gunshot wounds of the organ have been observed, the healing taking the form of a large, depressed, connective-tissue scar passing through the organ.

REPAIR IN THE KIDNEY.

The study of the healing of wounds in the kidney is of considerable surgical importance because of the frequency with which that organ is opened to search the pelvis for stones, or partially resected in the removal of tumors.

Simple incisions or needle punctures of the kidney when made parallel to the course of the vessels are primarily closed by the clotting of the blood exuded from the vessels injured by the instruments. The cells along the course of the wound, especially those which have had their nuclei injured, undergo immediate necrosis, evidences of which can be noted at the end of an hour (Fig. 81). Within a few hours the necrosis extends further through the renal tissues owing to a local anemia produced by the injury to the vessels. Leukocytes emigrate abundantly from the capillaries, and in thirty-six to forty-eight hours the regenerative process is very active. Mitoses are seen chiefly in the epithelium of the straight tubules which may partially regenerate (Fig. 120). The convoluted tubules, however, though their cells may divide, are incapable of forming normal tubules. In the course of two weeks the wound is firmly united by connective tissue which contains some atrophic glomeruli and a few renal tubules, the epithelium of which has undergone regressive changes with the production of a low, flat epithelium. Occasionally small retention cysts are formed from the new tubules.

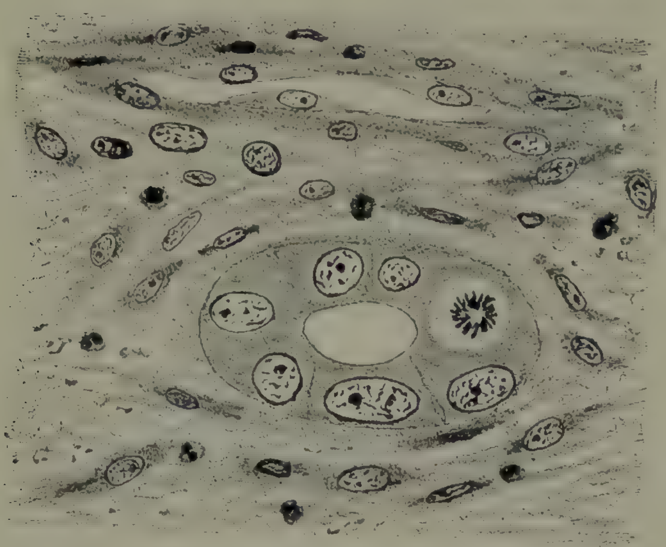

Fig. 120.—Repair in a Rabbit's Kidney, Five Days after Injury.

The drawing is made from an area just outside of the reaction zone shown in the photograph in Fig. 121. A new formed kidney tubule showing mitosis in one of its cells lies in a matrix of granulation tissue.

Large incisions, if made with a sharp knife and perpendicular to the convexity, wound only a moderate number of the transverse vascular arches and cause but a moderate amount of anemic necrosis. If, however, the instrument is not sharp, or if the incision is made obliquely or transversely to the course of the vessels, an extensive necrosis may result, healing only after the production of large amounts of scar tissue (Fig. 121).

A great deal of interest has recently been attached to the anatomic results following removal of the capsule of the kidney, especially since this procedure has been recommended by Edebohls as relieving some of the symptoms of chronic nephritis. That surgeon's opinion is that the blood-supply of the kidney is increased by the ingrowth of vessels from the newly formed capsule. The numerous studies which have appeared based upon the examination of both human and animal kidneys have shown that the removal of the capsule from a healthy kidney may incite an interstitial growth of connective tissue with damage to the tubules. The force required to strip the capsule from a kidney which is the site of a chronic diffuse nephritis very frequently gives rise to extensive hemorrhages in the cortical portion of the organ. These hemorrhages incite necrosis of the surrounding tissue and ultimately scar formation.

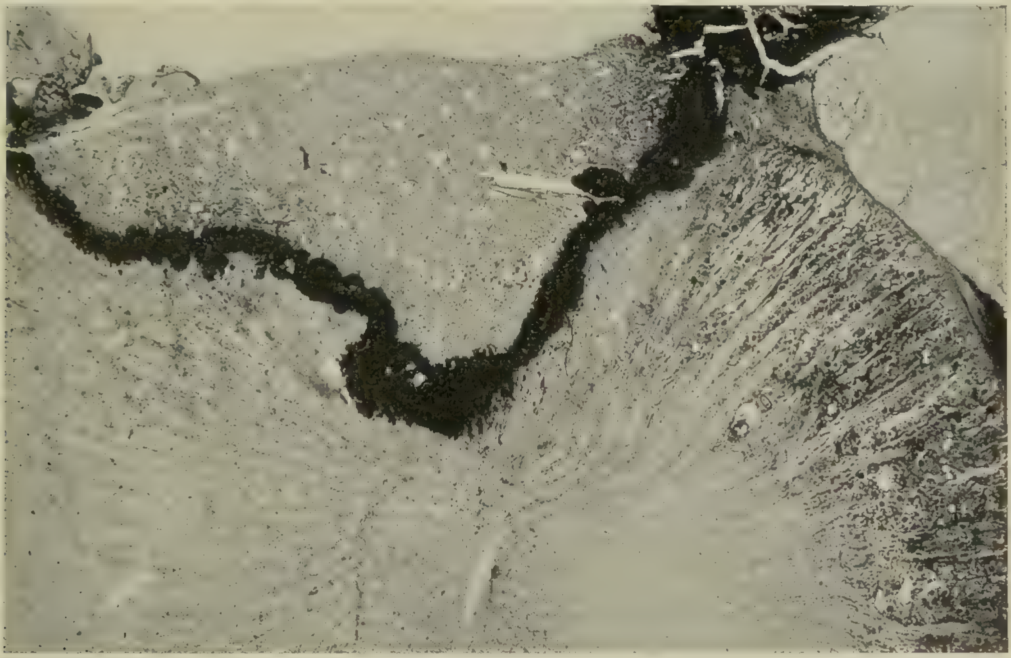

Fig. 121.—Aseptic Wound in a Rabbit's Kidney, after Five Days.

The incision has given rise to a considerable interference with the nutrition of a wedge-shaped area in the cortex. The irregular black line at the periphery of this necrotic area is composed of leukocytes and dead cells. Just outside of this, toward the healthy portion of the kidney, is a layer of granulation tissue which will ultimately close the wound.

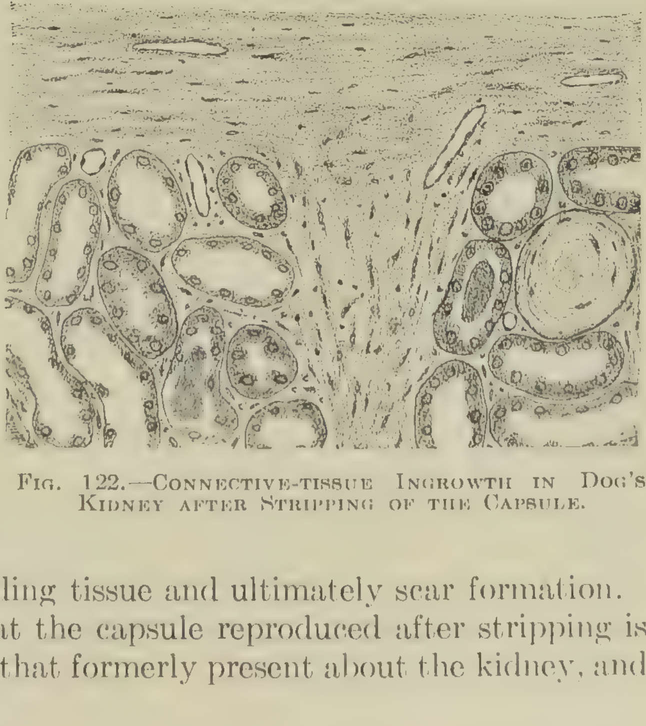

Fig. 122.—Connective-tissue Ingrowth in Dog's Kidney after Stripping of the Capsule.

It has also been noted that the capsule reproduced after stripping is often very much thicker than that formerly present about the kidney, and that the newly formed vessels which may anastomose with those of the kidney substance are ultimately occluded by the contraction of the cicatricial tissue. It has also been shown that the further development of the lesions of a nephritis either in animals or in man is not permanently influenced by the operative interference, although a temporary improvement in symptoms is not uncommon.

REPAIR IN THE PANCREAS.

The reparative power of the pancreatic tissue after injury is very slight and the condition is complicated by the action upon the tissues of the abdominal cavity exerted by the enzymes secreted by the gland. Any considerable trauma to the pancreas is apt, therefore, to result in the production of a more or less extensive pancreatitis with fat necrosis.

When healing does take place the repair is almost wholly by the new growth of connective tissue. The edges of the wound necrose, the dead tissues are removed by phagocytosis or absorption, and a new growth of granulation tissue fills the cavity, with the ultimate production of a scar.

REPAIR IN THE SUPRARENAL GLANDS.

The specific cells of the suprarenal gland possess practically no power of regeneration, so that healing of wounds in these organs takes place wholly by growth of fibrous tissue filling up the area which has been injured.

REPAIR IN THE UTERUS, OVARIES, AND FALLOPIAN TUBES.

Uterus.—Wounds of the uterine mucosa, such as may be produced by excising a small mural fibroid, heal very quickly by union of the edges of the incision by fibrin and blood-clot and later growth of connective tissue which gradually atrophies and is replaced almost completely by muscular fibers so that the site of the injury is difficult to determine after a few months have intervened.

Wounds in the wall of the pregnant uterus heal chiefly by agglutination of the edges by fibrin, and later by hyperplasia of the connective tissue. A very considerable regeneration of muscular fibers occurs and multinuclear giant cells, probably of placental origin, are found scattered in the neighboring tissues.

Wounds of the mucous membrane of the uterus need not be considered, except that form of injury which follows the removal of the mucosa with the curette. After such removal of the mucosa the injured surface is covered with fibrin and blood-clot under which a very rapid regeneration of the connective tissue and blood-vessels of the endometrium takes place. The glandular structures are regenerated from remnants of the tubules left in the deeper muscular layers, for it is well known that a few tubules penetrate deeply into the muscle, considerably beyond the depth usually reached in curettage. The tubular epithelium proliferates in a direction toward the cavity of the uterus, and when it reaches the surface spreads out in a flat layer of irregularly shaped cells, usually single, occasionally in several layers. The epithelium thus formed may line the uterine cavity very rapidly, even within five or six days (Werth). The complete restoration of the endometrium takes place under the epithelial layer and requires from four to six weeks.

Studies carried out by Bossi suggest the possibility of regeneration of the glands of the endometrium from small fragments of superficial epithelium which may have been left *in situ*, a similar phenomenon to that observed in repair of the mucous membrane of the stomach and intestine.

Ovary.—The healing of wounds of the ovary is of so little practical importance that details may be omitted here, but many studies have been devoted to determining the capacity of this organ to withstand transplantation with the idea of replacing diseased organs by healthy. Most of the experimenters have placed the transplanted organ in the folds of the broad ligament or in the intrauterine space. A proliferation of the surface epithelium of the peritoneum follows with the formation of vascular connective-tissue adhesions partly surrounding the ovary. Under these circumstances the organ remains morphologically normal and may contain normal follicles with egg cells and corpora lutea for four months. Whether such an ovary is capable of freeing ova and thus permitting pregnancy is still doubtful. The positive results reported in human beings are open to much criticism, though animal experiments have succeeded. It is certain, however, that such transplanted ovarian fragments prevent the atrophy of the uterus which would otherwise occur in animals from whom the ovaries have been removed.

Fallopian Tube.—Healing of the wall of the Fallopian tube is accomplished by the same procedures as that of the uterus and a very perfect regeneration of the tubal epithelium takes place.

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A complete record of all the papers consulted in the preparation of this article could not be included in the bibliography on account of lack of space. Only the most important papers, therefore, are given in the references. Very complete lists of monographs on the topics considered in the preceding chapter may be found in Ziegler's "Lehrbuch der allgemeinen pathologischen Anatomie," Jena, 1905; in Marchand's "Der Process der Wundheilung," Stuttgart, 1901; and in the files of the "Centralblätter for Pathologie and Chirurgie." Many important articles on repair and inflammation are contained in Ziegler's "Beiträge zur pathologischen Anatomie."

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CHAPTER X.

THROMBOSIS AND EMBOLISM.

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THROMBOSIS.

Definition.—Thrombosis is the act or process of formation of a thrombus, or the condition characterized by its presence (Welch). A thrombus is a mass, the component parts of which are derived from the blood, formed in the heart or peripheral vessels.

Pathogenesis.—According to their location thrombi are described as of arterial, venous, capillary, or cardiac origin, and according to their composition as white, red, and mixed thrombi. Then again from the clinical standpoint thrombi may be classified as simple or bland on the one hand, and infectious on the other. As to the pathogenesis of thrombi there may be said to be four factors, each of which plays a more or less active part in the thrombotic process: the presence of infective organisms, structural alterations of the intima, disturbances of the blood-current, and chemical changes in the blood. By way of preface it may be said that it is not necessary that all these factors should be operative in every case and, except in those cases due to infection, it is difficult to determine the relative degree of importance of the various etiologic factors. It is with infectious thrombi that surgeons have to deal most frequently. The causative factor in these cases is a pyogenic organism, the primitive lesion a phlebitis, and the terminal process a thrombosis or a thrombophlebitis. The thrombophlebites associated with such general septic processes as pyemia and septicemia were the first to be recognized as of infective origin; subsequently, however, the septic nature of thrombophlebitis has been admitted and recognized in other diseases of infectious origin, as in the various so-called infectious diseases. Among these may be included influenza, enteric fever, typhus, pneumonia, scarlet fever, variola and the like. Mention should also be made of the phlebitis not infrequently following operation upon the appendix and pelvic organs. Systematic bacteriologic examination at autopsies has revealed the fact that many thrombi associated with wasting and cachectic conditions, often spoken of as marantic thrombi, may be also of septic origin. The streptococci are the most frequent offenders; that is to say, in the majority of instances the specific organism, as of influenza or typhoid fever, has not been found in the thrombus, the latter having been the result of a secondary, often a streptococcic infection. In many cases bacteriologic examinations of the thrombi have yielded negative results, but this does not preclude the possibility or the probability of their infectious origin. Either the organisms have died, and will not therefore grow when transferred to suitable media, or, as assumed by French writers, the toxins become the active agents and give rise to the necessary inflammatory changes in the intima.

From what has been said it will be seen that infection is the predominant factor in the majority of cases of thrombosis which come under the surgeon's care. Brief reference need be made therefore to the remaining conditions, which play a part in the pathogenesis of this condition. First, as to the variations in the blood-stream. Retardation of the blood-current is but a predisposing or contributory cause. Unless in coöperation with some other condition, as a lesion of the vessel wall or the presence of organisms, it cannot give rise to thrombosis. If this were not so, the temporary closure of the carotid arteries, preliminary to operation on the face or head, would be in itself a very dangerous procedure. The rearrangements of the constituents of the blood, when the current is gradually slowed, as pointed out by Schimmelbusch, is now well known. The white blood-corpuscles accumulate in the periphery mingled with a few platelets, and as the current is still further retarded the white corpuscles in this zone diminish and the platelets increase. Of greater importance, according to von Recklinghausen, than the retardation of the current, is the peculiar whirling motion (Wirbelbewegungen) which is produced when the blood passes over an obstacle or from a dilated to a constricted channel, as, for example, in the case of aneurisms or in the dilated pouches of varicose veins.

Alterations in the structure of the intima are very much more influential than any variations in the blood-current. As examples of these may be mentioned the changes in the vessel wall that occur in contusions or wounds, in inflammatory lesions, and in such degenerative processes as atheroma, calcification, or necrosis. In this category may be included the thromboses, associated with endarteritis, which so frequently determine senile gangrene. The effect of these alterations of the structure of the intima is twofold, to some extent physical and to some extent chemical. Physical in that the normally smooth surface of the intima is replaced by one which is rough and adhesive; chemical in that the perverted cells of the intima liberate a fibrin ferment and thereby favor thrombus-formation. When these structural changes in the intima are such as to cause projections into the lumen of the vessel or partial obliteration of its lumen, they contribute further toward the elaboration of the thrombotic process by interfering with the velocity of the blood-current.

In concluding the discussion of the etiology, allusion should be made to the part played by chemical changes in the blood. Of these Welch says, notwithstanding the lack of a substantial basis of demonstrated facts for the opinion that human thrombosis is often caused by liberation of fibrin ferment in the general blood-stream, it would be quite unreasonable to suppose that chemical changes of the blood are without influence upon the occurrence of thrombosis in man. The precise effect of these chemical changes is as yet hypothetic. That they are important factors in the thrombosis of toxic conditions is undoubted. But whether by the liberation of fibrin ferment or by favoring the production of platelets and their subsequent viscous metamorphosis in still undetermined.

Pathology.—Thrombi are made up of the constituents of the blood in various proportions—red and white corpuscles, platelets, and fibrin. According to whether they form in circulating or stagnating blood they are designated as white or red thrombi respectively. The latter have little or no practical significance; they are composed of fibrin and of red and white corpuscles in the same proportions as in the circulating blood. The mixed or white thrombi, formed in circulating blood, are those with which, as clinicians, we have to deal. Blood platelets may be said to form the nucleus of the white thrombus, whatever elements it may contain at a later stage of its development.

If studied experimentally, the thrombus will be found to consist at first chiefly of platelets, which appear microscopically as pale or round bodies, though sometimes of irregular shape, and of variable size; of leukocytes, which though at first present in small numbers, in a short time begin to accumulate in increasing numbers until they constitute the predominant element, at first on the margins of the clump of platelets and subsequently infiltrating the latter. As to the origin of the blood platelets, it is believed by some that they exist normally in the blood, circulating with the red corpuscles, although more recently a number of observers rather favor the view that they are derived from disintegrated red corpuscles. However numerous the leukocytes may be at one stage of the process, they probably in no instance constitute the initiative factor. At a still later stage fibrin appears as a constituent, and, as in the case of the leukocytes, at first in the margin and later extending into the thrombus itself. To the naked eye the thrombus appears as a grayish-white, viscid, homogeneous mass. Under the microscope it will appear to be composed of areas of granular material, representing altered blood platelets, surrounded by leukocytes, fibrin, and a few red corpuscles.

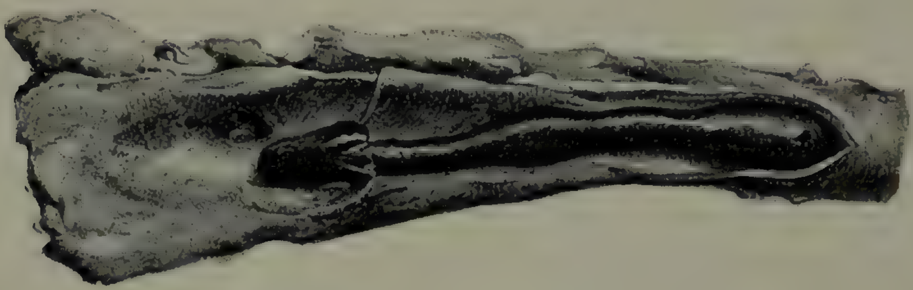

Fig. 123.—Thrombus of Femoral Vein (Warren).

So much as has been said of their structure applies to fresh thrombi. As time goes on they undergo certain well-defined changes, both as to size and structure. These changes consist essentially in the extension of the thrombus itself, in metamorphosis of its constituent elements, and finally in the organization of the thrombus. The time which may be required for the terminal or organizing stage is very variable, depending upon the general condition of the patient, the condition of the circulation and of the vessel wall itself, and upon the presence or absence of infection. The presence of pyogenic organisms may retard or altogether interfere with the completion of the process, leading rather to suppuration and disintegration of the thrombus. The lack of tone or vitality in the tissues of the vessel may exert a retarding influence, and any disease of the vessel wall must of necessity interfere with that active proliferation so necessary to the process of organization. The changes that occur in the constituency of the thrombi are varied. In some instances the leukocytes may accumulate in such large numbers as to become a predominating feature. Such thrombi are termed "leukocytic." At a still later stage the thrombus will be composed almost entirely of fibrin; the leukocytes undergo degeneration and the platelets are replaced by fibrin. Such thrombi are termed "fibrinous." In the smaller arteries and veins and especially in infective diseases more or less hyaline material will be found in the thrombus. This so-called "hyalin" thrombosis has been met with in spontaneous gangrene, in the liver and kidneys of subjects of infective diseases, and in the lungs in pneumonia. This hyaline material is derived from the various elements in the blood. Some thrombi undergo calcification and are thus converted into phleboliths or arterioliths. A case has been quite recently reported[1] (Clark) in which a phlebolith was found in the internal iliac vein. More commonly, however, they are found in the prostatic plexus of men and the pampiniform plexus in women.

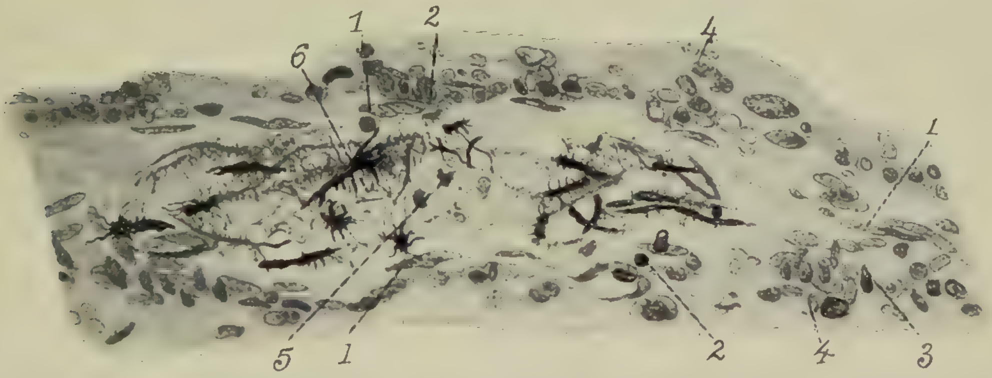

FIG. 124.—BEGINNING THROMBOSIS IN A SMALL ARTERY, FROM A CASE OF PURULENT FIBRINOUS LEPTOMENINGITIS (Alum cochineal; Weigert's stain; × 625) (Dürck).

1, Endothelium; 2, muscle-cells in transverse section; 3, muscle-cells in oblique section; 4, cells of the adventitia; 5, leukocytes within the lumen; 6, fibrin stars.

An old thrombus differs from a young thrombus in still other particulars; the leukocytes undergo fatty degeneration and necrosis, the red corpuscles become decolorized, irregular in shape, and pigmented; the hemoglobin dissolves and, becoming converted into hematoidin, gives the clot a brownish hue. The platelets may disappear entirely and be replaced by fibrinous deposits or they may persist as a finely granular or even homogeneous mass. Furthermore, some thrombi undergo a softening or liquefying process, which differs according as it is of infectious or non-infectious origin. In the latter instance a cavity will be found in the thrombus containing a thick opaque fluid, which is derived from the disintegration of the solid constituents of the thrombus, and not from an infectious process. The process has no connection whatever with bacteria, but it is attributed to the presence of a ferment. Of much greater significance is the softening due to the action of bacteria; examples of this will be met with most frequently in cases of thrombophlebitis of infectious origin. As a result partly of the action of the organisms in the thrombus and of the inflammatory process in the vessel wall, the thrombus undergoes liquefaction and breaks down into a reddish-yellow or greenish creamy substance, which consists of granular débris, pus cells, and microörganisms. It is in this septic variety of softening particularly that fragments become separated from the thrombi and as infected emboli (*vide* section on Embolism) are carried off by the circulation and deposited in the internal organs, usually the liver, kidneys, and lungs, where they give rise to secondary or embolic abscesses. It should be remembered, however, that in some instances an infected thrombus may be walled in by a coagulation extending beyond the infected portion of the vessel; the process then remains circumscribed.

The terminal stage in the process of thrombosis is the stage of organization. This expression—organization of thrombus—is in itself a misleading one, for as a matter of fact the thrombus entirely disappears and is replaced by fully organized fibrous tissue. The thrombus itself plays no part except in so far as in the rôle of a foreign body it, so to speak, initiates the process. It is quite possible for the lumen of a vessel to become obliterated permanently with a fully organized fibrous plug without the formation of a thrombus; such is the case when a ligature is applied to a vessel in continuity. In the process of organization the thrombus becomes infiltrated wth leukocytes; then follows a proliferation of fixed connective-tissue cells derived from the endothelium and from the other fixed cells in the vessel wall. New blood-vessels now begin to form, pervade the clot, and establish anastomoses with each other and occasionally with the lumen of the vessel itself both above and below the thrombus. The thrombus itself undergoes absorption and is replaced by embryonic connective tissue rich in blood-vessels. As the connective tissue becomes more fully organized it contracts and becomes converted into a fibrous plug. In some instances the contraction and retraction of the connective tissue occurs in such a way as to leave large blood-spaces lined by connective-tissue bands, and on still rarer occasions these bands altogether or in part disappear and the lumen of the vessel is restored wholly or in part.

The extension or growth of thrombi occurs in the direction of the blood-current; in the case of an artery the thrombus usually extends only to the next collateral branch above, although it may extend farther centrally and may also extend a little peripherally. Venous thrombi may extend, however, far beyond the original focus, even as far as the vena cava when originating in the veins of the lower extremity.

According to the nature and conditions attending their growth, thrombi are designated as follows: primary or secondary thrombi—primary when of local origin and remaining more or less confined to the point of origin, secondary when starting from an embolus; spreading, propagating, or continuing when they extend some distance away from the original focus; parietal or mural, in contrast to annular thrombi; partial or complete, *i. e.*, obstructive. Mixed or white thrombi, at first soft and viscid, become firmer in consistency, tougher and drier. They present the well-known laminated structure. According to Welch,[2] the stratification is not easily accounted for. The usual explanation that the thrombus is deposited in successive layers must be accepted with reservation. It is more likely that the red layers in the thrombus are formed by the blood entering spaces resulting from irregular growth, or from contraction of the thrombus. By the vis a tergo the blood may be forced into and split, as it were, the thrombus; in this way, too, the presence of the red layers may be accounted for. Attention has also been directed to the peculiar ribbed like appearance on the surface of the thrombus. Microscopically mixed and white thrombi present a trabecular structure; the trabeculæ, extending from the wall of the vessel in a tortuous direction toward the periphery of the thrombus and freely anastomosing with each

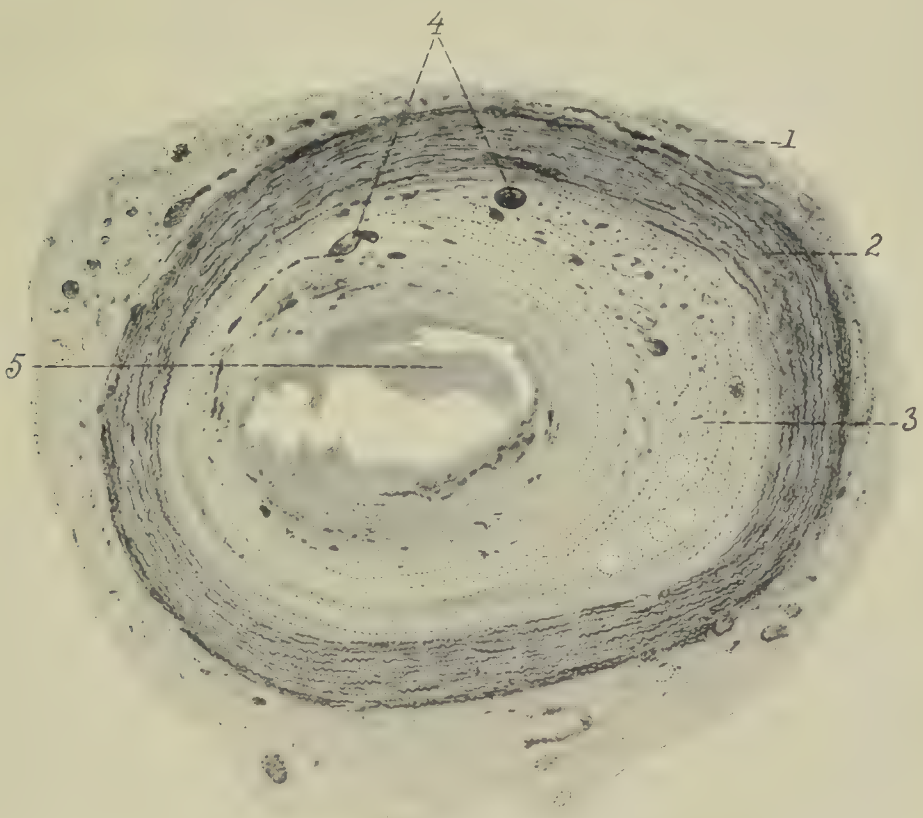

FIG. 125.—ORGANIZED AND PARTLY CANALIZED THROMBUS OF THE BRACHIAL ARTERY (Hemat.; orcein; ×32) (Dürck).

1, Adventitia; 2, tunica media; 3, organized thrombus—*i. e.*, replaced by connective tissue; 4, newly formed and in part dilated vessels within the thrombus; 5, disintegrated remains of the old thrombus.

other, are composed of platelets lined with fibrin and leukocytes. The intertrabecular spaces are filled with normal blood, in its fluid or coagulated state, or only of some of its constituents, particularly leukocytes and fibrin.

Thrombosis as Affecting Individual Vessels.—The Internal Jugular Vein.—Almost all cases of thrombosis of the internal jugular vein are of secondary origin. The greatest recorded number of cases of similar origin are those secondary to thrombosis of the petrosal or sigmoid sinuses in middle-ear disease. Baldwin [3] found in a series of 34 cases that 38 per cent. were secondary to middle-ear disease. As to the remainder, there was in sixteen a poor blood dyscrasia, three having carcinoma, six tuberculosis, two tertiary syphilis, one pyemia, one malaria, and two acute articular rheumatism. In but one instance did the morbid process seem to originate in the vein itself. In all the others it was secondary to thrombosis of the innominate vein or cranial sinuses. Alrich [4] collected eight cases in which there was thrombosis of the external jugular vein alone, associated with pulmonary tuberculosis. The diagnosis is not difficult; infiltration and edema of the tissues of the neck, cord-like induration of the vein itself, the appearance of a red band along the course of the vein, dilatation of collateral branches, and some restriction of the movements of the head are the characteristic symptoms. The head is usually held toward the affected side in order to relax the sternocleidomastoid muscle. When due to sinus disease the thrombus is usually limited to the upper third of the vein, and the prognosis should be guarded; when associated with sinus thrombosis the prognosis is very much graver because of the liability of pulmonary infarction. In all other cases thrombosis does not occur until the last stage of an otherwise fatal disease and has little or no effect upon the outcome. Only in those cases associated with sinus thrombosis must radical measures be considered. Owing to the possibility of the thrombus being propagated toward the heart or of septic pulmonary embolism, the internal jugular vein should be ligated or extirpated in every instance.

Thrombosis of the Mesenteric Vessels.—While occlusion of the mesenteric vessels was described as early as 1847 by Virchow, it was not until recent years that the subject was given the attention it deserved, possibly because of its infrequency, possibly because it was so seldom recognized. We are indebted to Oswald,[5] Corner,[6] Falkenberg,[7] and to Jackson, Porter, and Quinby [8] for their more recent studies and elaborate presentation of this subject.

Frequency.—As to the relative frequency with which the artery or veins are involved, Corner states that blockage of the arteries is more common than that of the veins in the proportion of 5 to 1, and that the involvement of the superior mesenteric artery bears as high a proportion as about 40 to 1, to that of the inferior mesenteric artery. This proportion may be an exaggerated one, however, since it is made from a study of only the fatal cases.

If we look to the blood-supply of the intestine, we will find substantial reasons for the superior mesenteric artery being the seat of the embolism in the great majority of cases. The superior mesenteric, through its branches, the inferior pancreatico-duodenal, the middle colic, the right colic, the iliocolic, and the terminal branches to the cecum and appendix, supplies no less than twenty-five feet of intestine and affords the only blood-supply to that region. The inferior mesenteric supplies only the descending colon, not even the rectum, which has several sources of vascular supply. The duodenum gets its blood-supply from two sources. From a series of experiments Litten[50] found that, physiologically speaking, the superior mesenteric artery was an end-artery, but that such was not the case with the inferior mesenteric or celiac artery. The enormous percentage of fatalities, therefore, after thrombosis of the superior mesenteric is thereby explained. There have been numerous theories advanced to explain the failure of a collateral circulation to become established, despite the fact that in the numerous arcades nature seems to have made provision for it. According to Litten, a higher blood-pressure is needed; to this Rosenbach [9] takes exception, and maintains that the normal blood-pressure is sufficient if there is a compensatory dilatation of the capillaries forming the collateral circulation. But this is interfered with by the violent intestinal contractions which occur in the seat of the infarct. Faber[10] attributes the failure on the part of the inferior mesenteric artery to maintain the circulation to fall of pressure in the superior mesenteric vein. The pressure in the portal system is lowered and the flow from the inferior mesenteric vein made so much easier that the blood from the inferior mesenteric artery follows its natural route rather than along anastomotic channels. There are, however, a number of cases, exceptional, to be sure, in which a collateral circulation has evidently become established. Such are the cases of Karcher[11] and of Chiene,[12] and Virchow reported two cases in which he found upon post-mortem that the main trunk of the superior mesenteric artery had been converted into an impervious fibrous cord. The intestines appeared normal.

The case of Chiene is still more remarkable. The specimen was taken from a female subject who had died from paralysis at the age of sixty-five years. There was an aneurism of the abdominal aorta and the inferior mesenteric artery which arose from the inferior part of the sac. The aorta was atheromatous, the celiac, with the exception of its first half inch, had been converted into a fibrous cord, both the superior and inferior mesenteric vessels were similarly converted into impervious fibrous tissue, so that practically the blood-supply of almost the entire alimentary tract had been interfered with. The branches of all these vessels, however, were patulous, and inasmuch as there were no changes in the stomach or intestine a collateral circulation must have been established. In commenting upon this case Chiene says: "This case is probably the only recorded example of an obliteration of the three anterior visceral branches of the abdominal aorta at their origins and of a consequent enlargement of the secondary anastomoses for the supply of the viscera, the stomach, liver, spleen, pancreas, and duodenum being supplied by the left lower intercostals and from the left renal and suprarenal arteries which inosculated with the lumbar arteries of the same side, the remainder of the intestine receiving its supply from the internal iliacs through a large plexus surrounding the rectum, except the cæcum and ascending colon, which received its blood-supply from the last dorsal artery on the right side."

Etiology.—All those conditions which lead to thrombosis of the other vessels may be factors in the causation of thrombosis of the mesenteric arteries and veins. Arteriosclerosis, endocarditis, atheroma of the aorta, are the most common causes of arterial thrombosis. According to Corner, it is most common in men past middle life and secondary to valvular disease of the heart, especially mitral disease. As to venous thrombosis, this may be primary or secondary to thrombosis of the portal veins. Delatour[13] reported a case in which the thrombosis of the mesenteric vein developed during the post-operative convalescence after a splenectomy. Almost immediately after the operation the patient developed a double pneumonia, and during the convalescence the patient was seized suddenly with an attack of severe pain in the abdomen and vomiting, with high fever and almost imperceptible pulse, and went into collapse, from which she did not rally. At the autopsy a thrombus was found in the splenic veins which were greatly distended and tortuous, the thrombus extending into the portal and mouths of the mesenteric veins. Whether or not the thrombosis was the result of the operation or was precipitated by the attack of pneumonia, must be conjectural. In another case, Johnson[14] attributed thrombosis to the deposits of tubercles about the tributaries to the vein in a case of tubercular peritonitis. The patient developed signs of intestinal obstruction; exploratory laparotomy was immediately performed and several ounces of clear, blood-stained fluid escaped. A coil of moderately distended small intestine was exposed and the mesentery was deeply congested and thickened.

These, however, are rare and exceptional cases. The most common causes include infectious conditions of the intestinal tract, including appendicitis, typhoid fever, general sepsis, as septicemia and puerperal fever, syphilitic phlebitis of the mesenteric vein, and phlebitis of the veins of the lower extremity. Secondary thrombosis is due to conditions causing stasis of the portal circulation, *e. g.*, cirrhosis and syphilis of the liver, septic lesions of the portal system, as pyelophlebitis, or it may follow thrombosis of the accompanying artery.

Pathology.—In contrast to what happens when the kidney, brain, or spleen are involved occlusion of the vessels in the intestine causes, as a rule, a hemorrhagic infarct; only in exceptional cases there will be an anemic infarct. Various theories have been advanced to account for these diverse manifestations, but none are satisfactory. An anemic infarct has followed closure of the artery only, on the one hand, as in the case of Grawitz,[15] and, vice versa, a hemorrhagic, and not as one would expect an anemic, infarct has followed simultaneous closure of both artery and vein, as in Taylor's[16] case. These cases are cited simply to illustrate the difficulty of attempting, as Sprengel did, to adopt a classification according as the arterial or venous supply is interrupted (hemorrhagic infarct), or the arterial supply alone (anemic infarct).

Whatever be the explanation of these phenomena, the effect upon the tissues has been frequently observed at operations and autopsies. Depending somewhat upon the duration of the disease, one may find only a simple hyperemia or absolute gangrene, perforation and localized peritonitis. This reservation as to the duration of the disease was made because there is such a wide variation in the rapidity of the process. In some cases, as those of the fulminating type, the most extensive gangrene may be present, within forty-eight hours, while in other organs three weeks may elapse before the intestine becomes gangrenous. We will refer to this again when speaking of the clinical aspects of the disease. In the majority bloody fluid will be found in the peritoneal cavity, the mesentery will be swollen and edematous with hemorrhages of various sizes between its layers, the mesenteric glands may be enlarged. The intestine itself

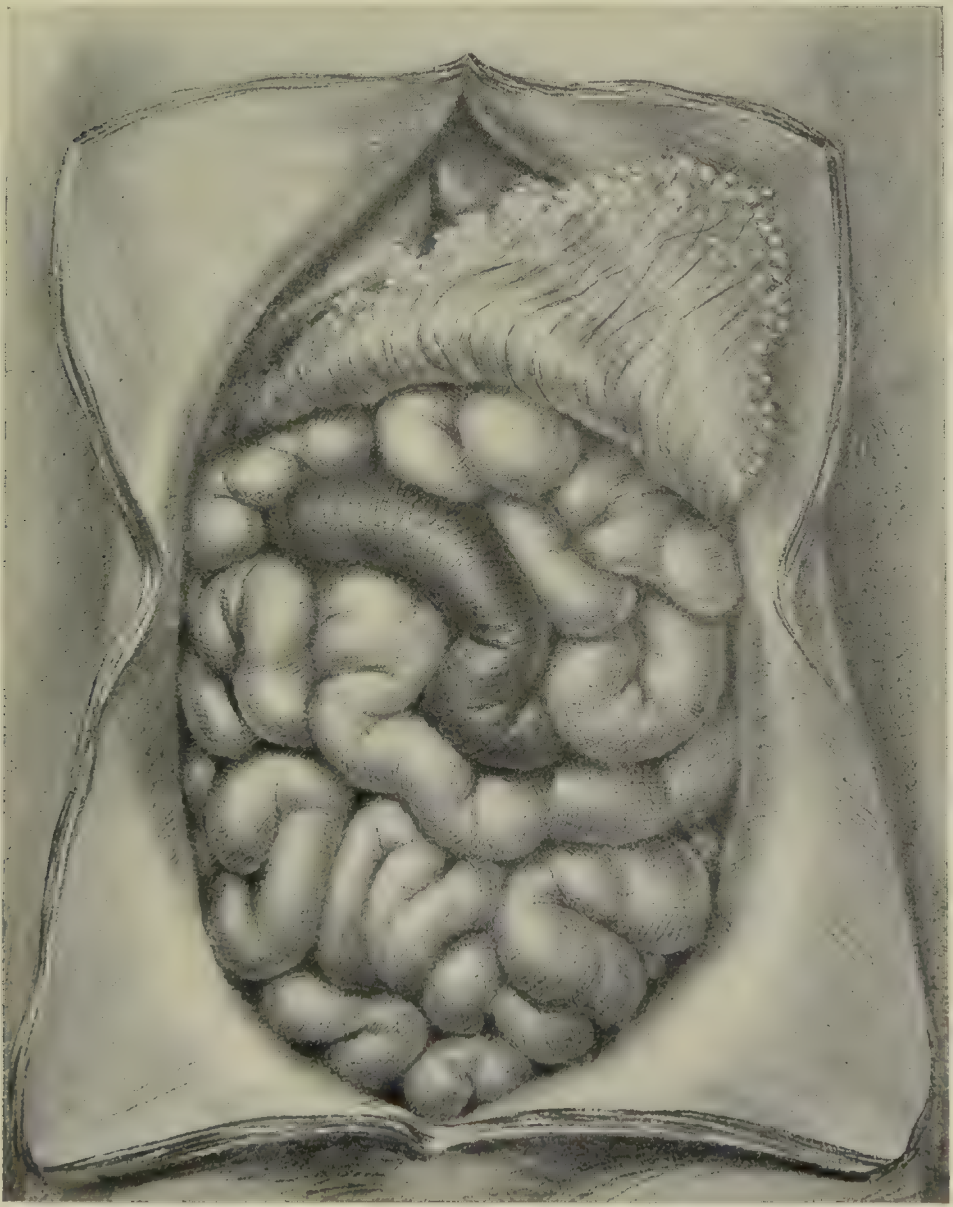

Fig. 126.—Illustrating the Appearance of the Abdominal Cavity in which One Coil of the Small Intestine was Totally Black, and yet was Surrounded by Other Coils of Normal Color (Kenerson).

will present the appearance of one or the other stages of gangrene [17] (Fig. 126); there may or may not be a line of demarcation; the intestinal mucosa will be the seat of extensive ulceration, involving sometimes its entire circumference; hemorrhagic areas will be seen in the serosa; the intestine itself may be distended and its contents in about two-thirds of the cases are bloody. The extent of the gangrenous area varies according as the inferior or superior mesenteric vessels are involved, and as the main trunk or one of its branches is the seat of obstruction. In a case reported by Ballance [18] the entire small intestine from the commencement of the jejunem to the cecum was involved. The thrombus had originated in the superior mesenteric and extended into the portal vein. On the other hand, more especially in the large intestine, a comparatively small section may be affected. Gangrene, however, is not always the sequel of a hemorrhagic infarct. There are cases in which the collateral circulation becomes established and resolution follows. The size of the infarct does not always affect the prognosis. A very small infarct may lead to gangrene and perforation, while an extensive one may undergo complete resolution.

Symptomatology.—Mesenteric thrombosis is a disease more prevalent in middle life, especially in the fourth and fifth decades. It is commonly met with in patients who are subjects of endocarditis or arteriosclerosis. It may run an acute, subacute, or chronic course. The initial symptom is pain, sudden in onset, usually diffuse though often localized, constant but with acute exacerbations. The intermittent character of the pain is attributed by some to intestinal contraction, although Schnitzler [19] believed it to be due to the local anemia that would follow the effect of a weak heart upon the blood-pressure. The early symptoms are not unlike those of acute intestinal obstruction, pain of a paroxysmal character associated with reflex nausea and vomiting. The vomitus is at first the normal contents of the stomach, but later becomes bile-stained, stercoraceous, and, if the lesion is high up in the small intestine, bloody. One of the most characteristic and significant symptoms is the passage of blood. In an analysis of 153 cases Jackson, Porter, and Quinby found that in 41 per cent. of cases blood was found in the stools. There may be diarrhea at first, but when the intestine becomes paralyzed there will be absolute constipation. Tenderness was found in 70 per cent. of cases and in 67 per cent. of these the tenderness was general. As a result of the complete intestinal paralysis which is due at first to the vascular stasis, later to the putrefactive process, the abdomen becomes distended. Intestinal obstruction almost inevitably follows; if it appears very early in the course of the disease it is no doubt the result of a reflex paresis of the intestinal wall; later the paresis is due to local nutritional disturbances and finally to a localized peritonitis. In fulminating cases the temperature is subnormal, but if the patient survives the early stages, reaction may ensue, and a rise in temperature will be recorded. As an example of the acute type of the disease the case of Fagge [20] may be cited: The patient was seized in the morning with violent abdominal pain and aggravated vomiting. In the course of a few hours she was in a state of absolute collapse, her pulse was almost imperceptible, the pain was paroxysmal, and she was vomiting blood-stained liquid. There was some amelioration of the symptoms, but later in the day an attack similar to the first occurred, and within a few hours the patient died. Among the symptoms which are less constant should be included rapidity of the pulse, extreme and unaccountable restlessness and excitability, leukocytosis, and glycosuria.

Diagnosis.—From a review of the symptoms it will be readily seen that there are a number of conditions which present a clinical picture so similar in one or the other of its stages as to make the diagnosis exceedingly difficult; acute perforative appendicitis followed by general peritonitis, volvulus, intussusception, acute intestinal obstruction from bands or internal hernias, all must be considered. A typical case of mesenteric thrombosis or embolism, according to Gerhardt, should present the following features: a source for the embolus, profuse intestinal hemorrhage unaccounted for by a lesion of the intestinal wall or obstruction to the portal circulation, the characteristic paroxysmal pains, ileus and the presence of fluid in the abdomen, a rapid fall in temperature, and the presence of a large palpable mass between the layers of the mesentery. Unfortunately, however, many cases exhibit but few of these symptoms, and a differential diagnosis becomes impossible. If there was neither bloody vomitus nor stools it would be almost impossible to distinguish the condition from acute intestinal obstruction. The condition which it most resembles is intussusception. Here the main point in the differential diagnosis is the age of the patient; 56 per cent. of cases of intussusception occur in young persons, and the majority of cases of mesenteric thrombosis occur at the age of heart disease and arteriosclerosis. In both there are bloody stools, in both symptoms of obstruction, and while in intussusception there is the sausage-shaped tumor, there may be in thrombosis also a tumor caused by hemorrhage into or edema of the mesentery. As to distinguishing between thrombosis of the artery and that of the vein, the presence or absence of cardiac failure, arterial disease, or evidences of embolism elsewhere must be taken into consideration rather than any distinctive difference occurring in the abdominal symptoms (Ballance). It is practically impossible to differentiate between thrombosis of the mesenteric and that of the portal vein. In so many instances, as a result of the propagation of the clot, both veins are involved.

Prognosis—The outcome of the disease will depend upon two contingencies: either the establishment of a collateral circulation or the prompt recognition of the condition and an immediate resection of the gangrenous area of gut. In a series of two hundred cases Jackson found a mortality of about 94 per cent. The gravity of the disease is not always measured by the acute or chronic nature of the attack. An adequate collateral circulation may be established in the most acute cases and fail eventually in the chronic cases. Nor is the extent of the process always an index of the gravity of the disease, since perforative peritonitis may develop even though a very small segment of intestine be involved.

Treatment.—Any form of treatment other than operative need not be considered. Spontaneous recovery occurs in a small percentage of cases, but the mortality of the disease is so high that operation should be resorted to unhesitatingly as soon as the diagnosis is established. Even by this means the lives of very few patients have been saved; in a series of forty-seven operations only four, or eight per cent., recovered (Jackson). The extent of the lesion does not preclude the possibility of recovery, since Elliot's patient recovered after resection of forty-eight inches of intestine. There might be more recoveries, according to Jackson, Porter, and Quinby, if the method of operating was modified. Heretofore the operations have consisted in a complete resection of the gangrenous segment. This method is open to criticism because of the time required in its execution, and because, when the line of demarcation has not formed, it is impossible to determine how much intestine should be removed. To overcome these objections an enterectomy followed by an enterostomy, rather than an enterectomy with immediate anastomosis, should be practised; the involved gut should be brought well out of the wound with sound margins at either end, and after resection the open ends should be fixed to the wound and well walled off with tampons. With this exposure any extension of the gangrenous process can be immediately detected. Unfortunately the diagnosis is often not made until the patient is profoundly toxic or in collapse; in other words, in a condition unfit for the depressing effect of a major operation.

Arterial Thrombosis of the Extremities.—Arterial thrombosis is very much more common in the lower than in the upper extremities. It may be sudden in onset, as when due to embolism or traumatism, or of slower formation when it is associated with disease of the arterial walls, as endarteritis and arteriosclerosis, and when it is the result of infective or chronic diseases. In some instances this is both an arterial and a venous thrombosis.

The usual termination of arterial thrombosis is gangrene, a gangrene of the dry rather than the moist variety. When the gangrene is of embolic origin the initial sign is violent pain at the point where the embolus has been arrested. It should be borne in mind, however, that this does not continue to be the highest point of obstruction, as a thrombus may be propagated upward some distance from the original focus. Certain characteristic changes will be noted in the color of the limb. At first it becomes suddenly white and pallid, later mottled in appearance and finally black. The local temperature will be subnormal, sensation will be lost, and the limb will become paretic. At the seat of the thrombus the vessel may be felt as an indurated, somewhat painful cord, and below the thrombus absence of pulsation will be noted always at first, although if a collateral circulation becomes established pulsation may return in the terminal vessels. The limb gradually shrivels and undergoes mummification.

The limitations of the gangrenous process depend altogether upon the location of the thrombus; thus, when due to a thrombus forming in and limited to the iliac or femoral arteries above the origin of the profunda femoris, gangrene may be limited to the toes and a portion of the foot, whereas in obliteration of the popliteal vessel gangrene will extend up to the seat of the thrombus. If the patient survives the immediate shock and does not succumb to the disease to which the thrombosis owes its origin, a line of demarcation will form between the vital and devitalized tissues. A fatal toxemia may occur if the gangrenous limb becomes infected, or death may result from extension of the gangrenous process and exhaustion.

Thrombosis as a Complication of Certain Diseases.—The Infectious Fevers.—*Typhoid Fever.*—As a complication of typhoid fever thrombosis may occur in the heart, arteries, or veins. Cardiac thrombosis is itself a rare complication, and when it occurs is the result of a secondary infection. Arterial thrombosis, though more frequent, is not by any means a common complication. As to its frequency, Keen[21] collected 43 cases of gangrene from typhoid fever, to which Westcott added 72 cases, and in addition 21 cases of arterial thrombosis without gangrene. In a series of 1420 cases Bettke[22] found but 4 cases, and these limited to the toes. It may be either primary or secondary. In Keen's excellent monograph he cites two cases in which the thrombus had formed in the arteries evidently secondary to an endocarditis. In one case there were fibrinous clots in both the primitive iliacs, the deep femoral, and the popliteal, the walls of which were healthy, and in the left auricle there were old fibrinous clots with endocarditis. In a second case, with gangrene of both legs, the autopsy revealed apparently healthy arterial walls with the femoral artery only partially obstructed with a thrombus, and the vessel below entirely free. There was, however, an endocarditis with clots in the heart and the aorta was obstructed from its bifurcation to a point above the origin of the inferior mesenteric.

Primary arterial thrombosis, that is, a thrombosis not of embolic origin, is unquestionably of bacterial origin, although the infecting organism may not be the typhoid bacillus. There is, however, abundant evidence at hand to prove in many cases the presence of the typhoid organism at the site of the lesion. Owing to the great preponderance of cases occurring in the lower extremity, it must be admitted that the greater sluggishness of the circulation prevailing in the lower extremities, as compared with other parts of the body, plays an important rôle in determining the site at which the thrombus develops. As Keen points out, this is true not only of arterial but of venous thrombi, and not only of cases complicating typhoid fever, as well as other infectious fevers, but also those of non-bacterial origin. As has been said, the great majority of cases occur in the lower extremity, and, in contradistinction to the distribution of venous thrombosis, when the left limb is more frequently attacked than the right, arterial thrombosis exhibits no predilection for one side or the other. The following tables, published by Keen, show the evenness on the one hand, and the disproportion on the other, of the distribution of arterial and venous thrombosis respectively:

	ARTERIAL GANGRENE.	VENOUS GANGRENE.
Both sides	12 cases.	7 cases.
Right side	25 "	23 "
Left side	24 "	69 "

Thrombosis may occur, however, in the vessels of the upper extremity, as well as in the cerebral, mesenteric, and pulmonary arteries and in the aorta. According to Orlowski, thrombosis of the abdominal aorta complicating infectious fevers has been recorded thirty-six times. He reported a case of a young man in whom, on the fifteenth day of the fever, symptoms of myocarditis developed. The patient died and the necropsy revealed a thrombus in the left ventricle and an embolus plugging the descending aorta.

As to the period of onset, the majority of cases occur in the second and third week. In Keen's series of cases there was none earlier than the fourteenth day and the latest was on the forty-eighth day. The effect of thrombosis, once established, will depend to a great extent upon the seat of the lesion. If in the cerebral, pulmonary, or mesenteric vessels, the issue is likely to be fatal. In the extremities the effects will depend upon the completeness of the obstruction and upon the freedom with which the collateral circulation may be established. It may be said, however, that in the majority of cases gangrene of the dry type occurs more frequently in the lower than in the upper extremity. Of 61 cases of arterial obstruction, tabulated by Keen, 46 were followed by gangrene.

Venous thrombosis is much commoner than the arterial form, partly because of the greater sluggishness of the circulation, partly, no doubt, because of the greater susceptibility of the vein to the invasion of micro-organisms. A phlebitis from any source is much more frequent than an arteritis. As to the etiology, the majority of cases are due to the typhoid bacillus, the remaining to a mixed or secondary infection.

In 1463 cases collected by Thayer[23] there were 41 cases of venous thrombosis. Of these, there was an undoubted associated infection in 7. In 40 instances the lower extremity was involved, in one the upper, and in one the pulmonary artery. The preponderance of cases occurring in the left side in this series corresponds with that in Keen's series. In 26 cases it was on the left side, in 5 on the right side, and in 9 on both sides. The femoral vein was affected in 21 instances, the popliteal in 5, the iliac in 5, the veins of the calf in 5, the internal saphenous in 3, the axillary vein in 1, the pulmonary artery alone once, and once together with the common iliac. Almost invariably the time of onset was in the third week or later, and the condition was ushered in with local pain and fever, the latter sometimes preceding the localizing symptoms. Pain is often of sudden onset, often the first localizing symptom, and referred to the course of the vein involved. Particular attention is called by Thayer to the sudden sharp abdominal pain associated with iliac thrombosis. This symptom occurring in the later period of the disease, associated with leukocytosis, should remind one of the possibility of the existence of iliac thrombosis. Chills were a common symptom, and in 15 per cent. of cases there was a leukocytosis of over 10,000; in two cases over 20,000. The degree of leukocytosis seemed to have some relation to the extent and severity of the lesion.

The results, immediate or ultimate, of venous thrombosis are not so serious generally as in the arterial type. In most cases the limb will be swollen, in a certain number edematous, and in a few instances gangrenous. When gangrene ensues it will be of the moist type, unless, as in some cases, there is a combined arterial and venous thrombosis, when the gangrene will be a combination of the moist and dry. There is, therefore, not only an immediate danger both of gangrene threatening loss of limb, and of sudden death following embolism of the pulmonary or cerebral arteries, but there is also the ultimate danger of more or less disability from continued disturbance in the circulation of the limb. Thayer examined a number of cases of venous thrombosis several years after recovery from typhoid fever, and found that when the femoral or iliac veins were involved, the affected extremities were usually considerably and permanently enlarged, with extensive varices often terminating in ulceration. In addition there were marked weakness of the limb, and cramps, especially at night and after over-exertion. When the thrombus involved only the popliteal veins the disturbance was less marked; when the femoral veins were the seat of the thrombus the collateral circulation was established with the iliac vein on the opposite side. There were marked varicosities over a triangular area the apex of which was a little below the umbilicus. The blood flowed from the affected thigh to the apex of the triangle and then down again to the inguinal ring on the opposite side, giving rise to marked varicosities, apparent on the surface of the abdomen (Fig. 127); in two cases in which both iliac veins were involved there were most extensive varicosities in both legs and thighs extending up over the abdomen and anastomosing with the internal mammary veins and other veins in the axilla. Nauwerck[24] reported a case of sudden death in a case of thrombosis of the left iliac vein. An embolism of the pulmonary artery occurred suddenly while the patient was straining, and death occurred ten minutes later. Another case is on record (Boaley[25]) in which the patient died of syncope; the thrombus extended from the iliac vein to the inferior vena cava and right auricle. The extent of the thrombus in this case, as in many others, is characteristic of venous as compared with arterial thrombosis. Keen cites four cases in which the clot extended into the vena cava, in one of which (Mackintosh[26]) the patient recovered. The collateral circulation in this case must have been established through the internal mammary, superficial epigastric, external pudic, internal saphenous, and circumflex iliac veins on both sides.

Before concluding the manifestations of thrombosis in typhoid fever, brief mention should be made of those cases in which perhaps only the terminal portions of the peripheral vessels are involved. Thus, for example, there have been cases, terminating in gangrene, involving only the toes, when the thrombus has not extended even as far up as the dorsalis pedis and the arteries above were free. Then, again, there are cases in which the ear, the nose, and portions of the face, neck, and trunk are involved and have been the seat of gangrene the origin of which could no doubt be traced to a thrombus in one or more of the peripheral vessels. Deserving of especial mention is that group of cases in which the genitalia and the perineum become gangrenous. The female genitalia are attacked much more frequently; irritation of the urine and feces, in patients who are suffering from inattention and neglect, perhaps may be considered a predisposing factor. There may be more or less extensive sloughing of the external genitalia, with subsequent contraction and perhaps closure of the vaginal orifice, or the condition may be confined to the vagina and lead to the formation of vaginal ulcers with more or less destruction of tissue and the establishment of vesicovaginal or rectovaginal fistulas. Keen has collected 14 cases in which the perineum was involved, seen mostly in

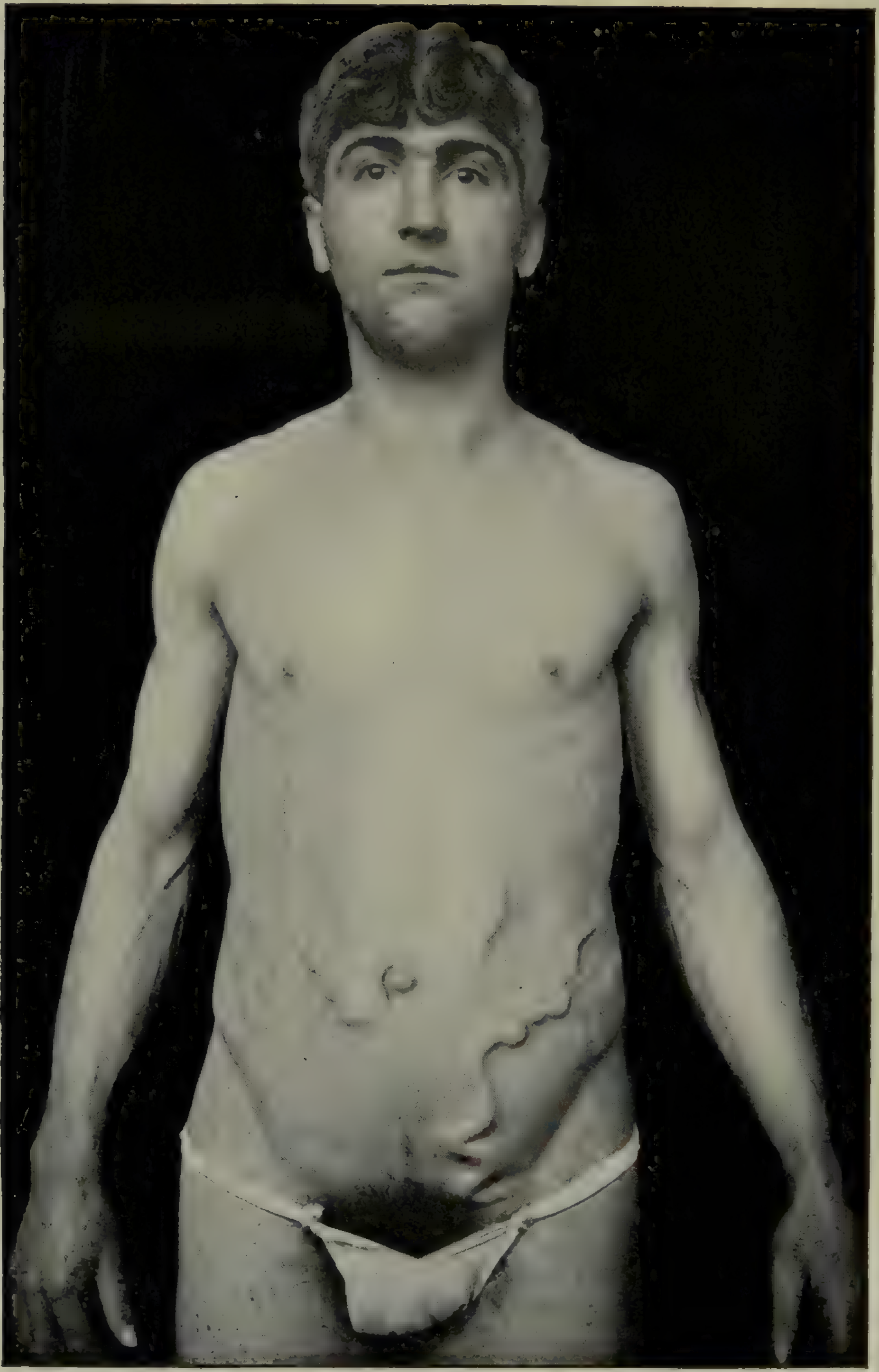

FIG. 127.—ABDOMINAL ARTERIES IN A CASE OF DOUBLE ILIAC THROMBOSIS OF TYPHOID ORIGIN (W. S. Thayer).

women as an extension of the process from the vulva. In many of these the tissue disintegration was so great as to establish direct communication with the rectum, and in many also perineal fistulas formed.

Tuberculosis.—By far the most common manifestation of thrombosis associated with tuberculosis is the peripheral venous thrombosis met with in the advanced stages of phthisis. According to Dodwell,[27] about 3 per cent. of phthisical patients develop this lesion. As to its etiology there are several hypotheses. Usually, however, the thromboses complicating phthisis have been regarded as of the cachectic type, but there have been enough positive reports of the bacteriologic findings to prove that thrombosis may be due directly to the invasion of microörganisms, more commonly micrococci, exceptionally the tubercle bacillus alone. Dodwell is disposed to attach more importance to structural changes of the vessel wall, probably the result of the secondary septicemia, than to an enfeebled circulation. While the peripheral veins are the most frequent seat of the thrombus, cases have been reported in which other veins were involved. Arterial thrombosis is a very rare complication of tuberculosis. It has been demonstrated, both clinically and experimentally, that tubercle bacilli circulating in the blood may invade the endothelial layer of the blood-vessel, but here, as in the case of venous thrombosis, the pyogenic organisms of the secondary infection, as well as certain circulatory disturbances, may unquestionably play some part. While the pulmonary artery is the seat of the thrombus in the majority of cases, it has been found at times in the femoral, the axillary, and the subclavian.

Pneumonia.—It is only of recent years that much attention has been paid or many observations made of thrombosis associated with infectious fevers. This is particularly true in the case of pneumonia. Da Costa,[28] who had reported the first case in 1894, published another paper in 1898 containing the reports of nine cases. Since that time a number of additional cases have been reported. While many cases no doubt have never been published, it must be admitted that thrombosis is an infrequent complication of pneumonia. Of 949 cases in the Boston City Hospital, Sears and Larrabee[29] were able to find but ten instances of thrombosis. The infrequency of thrombosis in pneumonia, a disease in which there is an increased fibrinosis, serves as an argument to refute the old idea that fibrinous conditions of the blood increased its coagulability. Da Costa attributed the thrombosis to a primary infective phlebitis and, despite the fact that the specific organism has so seldom been isolated from the thrombus, this theory is the most plausible and the one generally accepted.

In so far as its general manifestations and characteristics are concerned, the thrombosis of pneumonia differs in no respect from that of other infectious fevers. Suffice it to say that it is rather a sequel than a complication, and an unusual one, coming on during the convalescence rather than during the active stage of the disease; that the lower extremities are almost always involved, and the femoral oftener than any other vein; that there is the usual preponderance of cases on the left side and that the mortality is not inconsiderable. Of 41 cases 9 died, and in 5 of these death was due to pulmonary embolism. The following is a table of the location and distribution of the thrombus in a series of 22 cases tabulated by Steiner[30]:

Left femoral vein alone	6
Left femoral and internal saphenous	1
Left internal saphenous	2
Left external iliac femoral and int. saphenous	1
Right femoral	2
Right and left and left int. saphenous	1
Right internal saphenous	2
Right popliteal	2
Both femorals	4
Common iliacs at bifurcation	1

Influenza.—As a complication of influenza, thrombosis is not at all uncommon, and especially is this true of arterial thrombosis, which is more common in this than in any other acute infection. As to its etiology there is more or less speculation. According to von Leyden,[31] thrombosis is due to the disintegration of the white blood-elements. Gerhardt attributed the gangrene in his case to an extraordinary spasm of arteries; Kuskow,[32] however, found distinct changes, some degenerative and some proliferative, in the endothelial lining of the vessel wall; finally, Flexner[33] revealed the influenzal bacilli of Pfeiffer in the thrombus itself. While no specific cause can be demonstrated in many cases, and therefore the term marantic might seem applicable, still, in view of the fact that organisms and definite structural changes have been found in the thrombus or vessel walls, there is a growing sentiment, which is particularly outspoken in French writers, in favor of infective arteritis and phlebitis as the essential etiologic factor. According to Sansom, this complication is rarely met with in sporadic cases; it is more apt to appear in epidemics, in the more severe cases, and just when the temperature is about to fall; the pulmonary complications, bronchitis and bronchopneumonia, seem to favor the production of a phlebitis, though other complications, such as otitis media, endocarditis, or nephritis, may have preceded it. Teissier reported two cases and Orlando a third in which the thrombus formed while the patient was convalescent from a pneumonia complicating influenza.

The onset is usually sudden and follows rather than accompanies the disease. In a collection of cases of arterial thrombosis Welch [2] found the popliteal artery occluded in 6, the femoral in 4, the iliacs, axillary, brachial, pulmonary, and renal each in two, the central artery of the retina in one; the cerebral arteries were repeatedly invaded. The prognosis of arterial occlusion is more unfavorable in the lower than in the upper extremity; in the former instances gangrene occurred in every instance but only irregularly in the latter. As in Gerhardt's case, which he attributed to arterial spasm, so in a number of others a symmetric gangrene developed. Venous thrombosis is not at all uncommon as a complication of influenza; there is little tendency for both sides to be affected in the same individual; there is, however, a greater tendency, as compared with other infectious fevers, for it to appear in the upper extremity; whenever the thrombosis appears the influenzal symptoms seem to be checked. The outcome is usually not serious; the condition is, relatively speaking, benign and of short duration. The thrombus is situated, as a rule, in the femoral vein, less frequently in the superficial veins of the lower extremity, in the veins of the upper extremity, and occasionally in the cerebral sinuses.

Post-operative Thrombosis.—The development of a thrombosis or a thrombophlebitis during the post-operative convalescence after celiotomies, while not of frequent occurrence nor always of grave consequence, has excited the interest of the surgeons chiefly because of the obscurity of its origin. That it is not a common complication is evident from the fact that in some 3000 celiotomies Clark was able to find record of but 35 cases of thrombosis. In a series of 7130 gynecologic operations Schenck [34] found but 48 cases complicating the following operations. The operations were as follows :

Perineal alone	4
Hysteromyomectomy and myomectomy	19
Ovarian cysts	9
Hysterectomy for carcinoma	5
Suspension of the uterus	3
Suspension of the uterus with repair of the perineum	4
Hysterectomy for pelvic inflammatory disease	1
Miscellaneous	3

Albanus [35] found but 53 cases in 1140 laparotomies, and of this number 26 were in non-septic cases. The remaining 18 included 6 cases of pyosalpinx and 12 cases of septic lesions of the abdominal cavity.

Etiology.—According to Albanus, there are four factors which may play some part in the etiology of this condition: First, any disturbance of the venous circulation which might exist before the operation and would predispose toward thrombosis, as, for example, heart lesions, varicose veins, exhaustion, prolonged decubitus, and pressure of abdominal tumors. Secondly, conditions attending the operations, such as unavoidable chilling and exposure of the contents of the abdominal cavity and possibly traumatism to the vessel walls. Thirdly, the injurious effects upon the heart-muscle of the anesthetic, and, lastly, the topographic relations of the vessels. It is readily understood how a distended and overloaded sigmoid flexure might make pressure upon the left iliac vein, and others, particularly Riedel and Gerhardt,[36] call attention to the pressure exerted by the iliac artery upon the iliac vein.

Clark,[1] after careful investigation based upon clinical and experimental observations, has come to the conclusion that a post-operative thrombophlebitis is due to the effect of traumatism exerted upon the deep epigastric arteries during the course of the operation. The primary thrombosis originates in the deep epigastric vein and is slowly propagated along the line of the vessel until it reaches the external iliac vessel, where it gives rise to a retrogressive thrombus in the femoral vein. The arguments advanced in support of this view are so convincing as to warrant a brief outline of them. The theory that the lesion is attributable to traumatism or infection of the pelvic tissues is not tenable because this complication never arises, even after the most extensive operations upon the perineum, vagina, cervix, or rectum. That the lesion is of infectious origin would seem at least improbable on the following grounds: Of 41 cases there were but 2 following salpingo-oöphoritis, the overwhelming majority were surgically clean cases; the process was essentially a slow one, without mortality and unattended with the characteristic increased frequency of pulse—the pulse curve of Singer—which is rather pathognomonic of an infectious phlebitis. Inasmuch as the thrombosis never follows a pelvic operation unless a celiotomy is made, some factor peculiar to the abdominal incision must be sought for an explanation. This explanation lies in the close relationship of the deep epigastric veins to the abdominal incision. It will readily be seen how easily those vessels could be injured by strong retraction of the edges of the wound. A relatively large proportion of cases occur in the operation for the removal of large tumors and for suspension of the uterus where the ligatures might include or at least make traction upon these veins; the long interval —eight to fifteen days— between the operation and the appearance of the femoral thrombosis suggests a slow process starting some distance away. That the thrombus appears most frequently on the left side is attributed to the mechanical conditions on the left side which slow and derange the femoral and iliac circulation. Were it not for the fact that the anastomosis between the right and left epigastric veins is so free, the femoral vein would be reached more frequently by the thrombus, for it is more than likely that thrombosis frequently occurs in the epigastric veins after operations, even though it so seldom extends beyond. Perhaps the most striking proof of the theory expounded by Clark was presented in a case in which it became necessary to perform a second celiotomy. After the first operation the patient had developed a typical thrombophlebitis, and at the second operation both epigastric veins were found to be tense, hard, and as large as goose-quills, while one of these was decidedly varicose and contained a number of phleboliths.

The femoral vein is almost invariably the seat of the thrombus and the majority of cases occur on the left side. Of the 53 cases cited by Albanus, all but one involved the femoral vein; and of 38 cases of the series collected by Riedel, 16 were on the left side, 11 on the right, and 11 on both sides. In exceptional instances other vessels than those of the extremities may be involved; thus Maylard [36] reports a case of thrombosis of the mesenteric veins after gastrojejunostomy. The patient was a young female who had a ventricular systolic murmur and a very rapid pulse before the operation.

The condition does not make itself manifest, as a rule, before the eighth, more frequently on the fifteenth day. It is seldom preceded or accompanied by fever and in many instances the temperature maintains a normal or approximately normal course, seldom rising above 101° F. or, at the extreme, 102° F. The pulse, too, is but little if at all disturbed. Schenck called attention to the fact that in 41 per cent. of the cases of his series there was an albuminuria, whereas in 50 consecutive cases of operation for myomata and ovarian cyst where uncomplicated by thrombosis there were but 20 per cent. of cases showing albuminous urine. The prognosis will depend somewhat upon the treatment. If rest is not enforced for a considerable period, five weeks or more, the danger of pulmonary embolism is not inconsiderable. In two of Schenck's 48 cases pulmonary embolism occurred, but both patients recovered. The circulatory disturbance in the limb may entirely disappear or in some cases continue for an indefinite period.

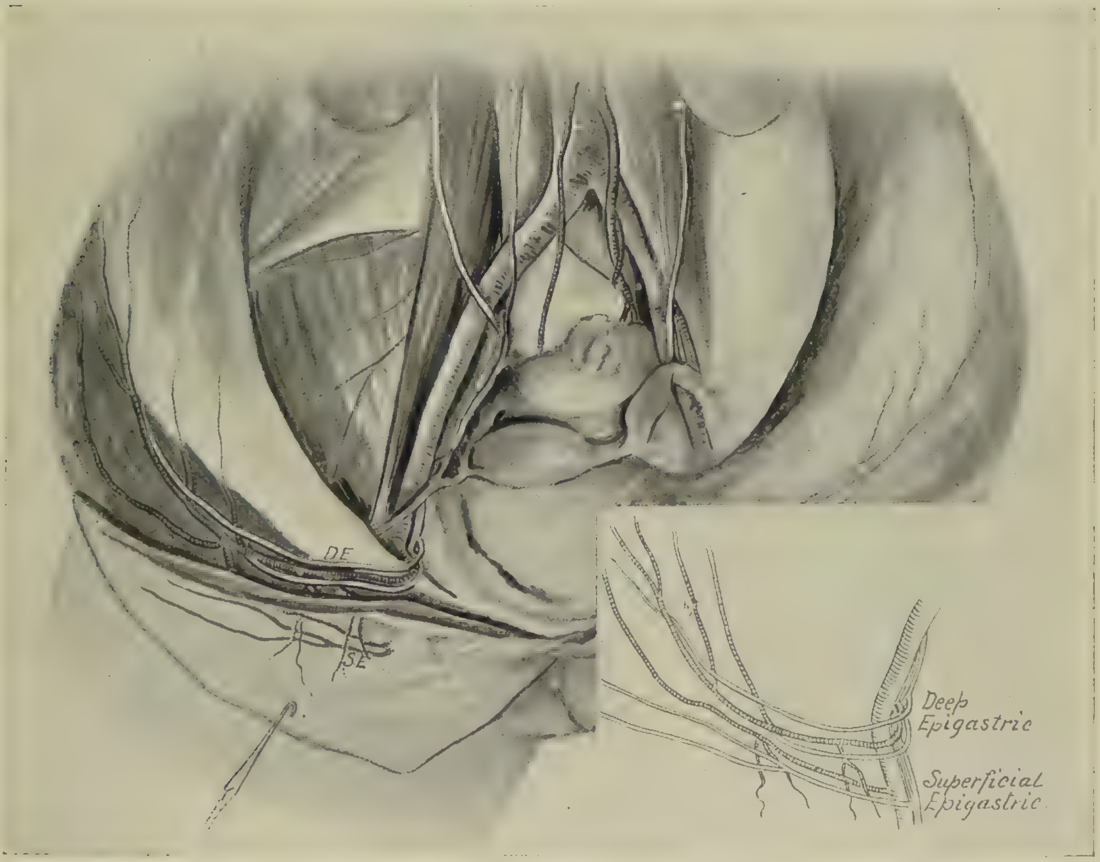

Fig. 128.—Showing the Relationship of the Deep and Superficial Epigastric Veins to the Linea Alba.

A median incision has been made, the walls turned back, bringing into view the deep epigastric vessels. On one side they have been exposed by dissection, on the other they are seen through the translucent peritoneum. They lie from three-fourths to one inch from the median line. There is some little variation in their position relative to the linea alba. In their course downward they run beneath the rectus muscle until the lower third is reached, when they perforate the transversalis aponeurosis and run outward beneath this structure and the peritoneum until the iliac vein is reached, around which they curve and enter the vessel at right or obtuse angle to the blood-stream. On each side there are, as a rule, two veins (venæ comites) which run singly throughout their course or unite before entering the iliac vein (Clark).

As soon as the thrombus has formed the limb should be elevated to encourage the venous circulation, wrapped in cotton, and surrounded with hot-water bags in bottles. The limb must be examined carefully day by day for signs of gangrene, and if the latter sets in, the greatest care must be taken to prevent the tissues from becoming infected. When the line of demarcation forms an amputation must be performed. When a collateral circulation is established, sufficient to maintain the circulation of the limb and prevent gangrene, absolute rest must be insisted upon, as a precaution against secondary embolism, until the clot has become thoroughly organized. From three to four weeks should be allowed for this process.

Appendicitis.—Thrombosis, as a complication of appendicitis, is not an infrequent condition, and may occur at any time in the course of the disease, with any variety of the disease and before or after operation.

Frequency.—A very fair estimate of the frequency of this complication is to be had by consulting the reports from Sonnenburg's [37] clinic. In a series of 1000 operative cases from this clinic there were twenty cases of thrombosis, distributed as follows:

Right leg	9
Left leg	6
Both legs	2
Vena porta	2
Vena cava	1
	20

A further analysis of this paper elicits some interesting facts, especially with reference to the time the complication develops and as to the pathologic nature of the process to which it owed its origin. Of these 20 cases, 14 occurred in the interval between the attacks and 6 during the attack. As to the nature of the process, we find that 9, or a majority, followed simple (catarrhal) appendicitis, 4 the gangrenous, and 7 the perforative type. The thrombi were distributed as follows:

Left saphenous vein	1
Right saphenous vein	2
Left femoral vein	5
Right femoral vein	7
Both femoral veins	2
Vena cava	1
Portal vein	1
Thrombophlebitis	1
	20

Lower extremity		17
Right side	9	
Left side	6	
Both sides	2	
Vena cava		1
Portal system		2
		20

To summarize the statistics we find that in this series all of the cases of thrombosis occurred in the veins, the majority in the veins of the lower extremity, and more on the right side than on the left, more cases in simple appendicitis than in any other one variety. The artery may, however, be the seat of the thrombus, as in Middledorpf's [38] case—a case in which there was an unopened appendical abscess. A thrombus, secondary to embolism, formed in the right femoral artery, and the limb soon became gangrenous and was amputated.

Etiology.—It is not improbable that the principal factor in the etiology of thrombosis after appendicitis is sepsis or infection. There are, no doubt, other contributory factors, such as those which were mentioned in the discussion of the etiology of thrombosis in general, but in the case of appendicitis we are dealing with a process which is essentially an inflammatory one, and one in which during its active stage thrombi form not only in the veins of the portal system, but in the veins emptying into the vena cava. As we will come to see (*vide* pulmonary embolism after appendicitis), the very fact that pulmonary embolism occurs as a sequela of appendicitis would seem to prove that the emboli must have arisen from thrombi in the tributaries of the vena cava and not of the portal vein. Riedel and others lay a good deal of stress upon ether as an etiologic factor, particularly in those cases which develop almost immediately, that is, within a day or two after the operation.

Results.—The prognosis in cases of thrombosis generally should be guarded, since there is always the danger of pulmonary embolism. Thus, of four cases reported by Riedel,[39] one died of pulmonary embolism, and in Sonnenburg's series of 1000 cases there were three deaths from embolism and two from pneumonia probably the result of embolism. But there is an added danger of thrombosis complicating appendicitis, namely, pyelophlebitis, a condition deserving special consideration.

Septic Pylephlebitis and Secondary Infection of the Liver following Appendicitis.—These are not as infrequent complications as commonly supposed. The first description of a case in which a perityphilitic inflammation was followed by pus in the portal vein and liver abscesses is attributed by Loison [40] to Waller [40] in 1846. In 1849 Hilliaret [40] described a case of ileocecal abscess in which all the hepatic veins were filled with pus, and again in 1854 Buhl [40] reported a case of similar origin in which there were multiple abscesses of the liver.

In 1187 cases of appendicitis operated upon at the Mt. Sinai Hospital in the course of ten years Gerster [41] met with the condition nine times. In 17 cases of liver abscesses in which the infection was through the portal vein, occurring at the Presbyterian Hospital (N. Y.), Hart [42] found 3 having their origin in an appendicitis. Munro [43] reported 9 cases of portal infection following appendicitis, and a number of other series and individual cases could be cited to emphasize the fact that this complication is not a rare and exceptional one.

The origin of pylephlebitis complicating appendicitis is not so difficult of explanation, if one takes into consideration these two facts: first, that in the course of an appendicitis, thrombosis of the veins of the appendix is but one of the manifestations of the inflammatory process, and, secondly, that there is a direct communication through the superior mesenteric vein between the veins of the appendix and those of the portal system. Curiously enough, this complication is just as likely to occur after simple and uncomplicated cases as in those of the most malignant type. Cases have been reported in which the complication arose after operations in the interval as well as during the acute stages or in the presence of an abscess. As Thompson [44] pointed out from his study of a series of cases at the Boston City Hospital, the pathologic processes in the appendix and the infectious organisms differed in no way from the processes or organisms found in uncomplicated appendix cases. The possibility of this very fatal complication arising, even when the operation is performed in the interval, at a time when the lesion is believed to be at least quiescent, should remind the surgeon of the responsibility he incurs in recommending operation.

Pathology.—The primary thrombus is usually found in the lower course of the portal vein, extending either continuously or interruptedly at short intervals toward the liver. These thrombi may involve the entire circumference of the vein, but more frequently are of the mural type. The completely obturating thrombi, according to Gerster, are generally found near or about the entrance of the portal vein into the liver, either in the trunk, which is rare, or more commonly in one or the other or both of its branches. In Thompson's series of cases the portal vein was filled with pus or occluded by purulent thrombi. In 5 of the 8 cases the mesenteric veins were involved, and in one case the vein running from the appendix was filled with pus while the other veins of the mesentery were normal. The inevitable consequence of thrombophlebitis of the portal vein is abscess of the liver. Emboli become dislodged from the thrombi from various causes, the larger ones to be arrested in the main branches of the portal vein, the smaller ones to enter the finer ramifications and even the capillaries. According to Bernard,[45] emboli may pass through the substance of the liver by way of the anastomosis between the portal vein and vena cava. Unfortunately the resulting abscesses are usually multiple, so that the possibility of being able to effect a cure by surgical measures is remote; though they may be situated in any portion of the liver, they seem to show some predilection for the anterior superior surface of the right lobe.

Symptomatology.—Severe and irregular chills followed by a rapid rise of temperature coming on shortly after an appendicectomy, even after an interval operation, performed presumably in the absence of an active infective process, should make one apprehensive of infective thrombophlebitis. The diagnosis is more easily made if, in addition to these symptoms, there is pain and tenderness over the trunk of the portal vein, that is, along the right border of the right rectus abdominis, tenderness over and uniform enlargement of the liver with in some cases fleeting jaundice, enlargement of the spleen, and rapid emaciation. The case may run such a rapid course that the complete clinical picture may not have had time to develop and the true nature of the process will not be recognized except at the necropsy. Some of these cases when terminating fatally may be attributed to an acute septicemia, in which it is assumed that the infectious process is in the peritoneum. Jaundice is by no means a constant symptom, and though the liver is almost always enlarged, pain and localized tenderness may be absent. According to Bryant,[46] pylephlebitis has been confounded with pyemia, septicemia (not due to portal infection), typhoid fever, malaria, adhesive pylephlebitis, chronic cholangitis, biliary calculus, and cirrhosis of the liver.

Taylor[47] says it is important to note whether or not there exists a malignant endocarditis, and Chvostek[48] has called attention to the possibility of confusing pylephlebitis with such thoracic conditions as pneumonia, empyema, and subdiaphragmatic abscess. The prognosis is in all cases grave; the factors which affect the prognosis most intimately are the virulence of the infecting organism and the presence or absence of multiple lesions in the liver. If the organism is an exceedingly virulent one, the case will run a rapid course and may terminate in forty-eight hours; with organisms of a lesser degree of virulence the course will be a more protracted one. Were it not for the fact that in such a large percentage of cases there are multiple abscesses of the liver the outlook would not be so hopeless. The futility of operating on a case in which the liver is riddled with abscesses need only be mentioned. It should be borne in mind, however, that in some instances[49] a single abscess has been drained and the patient recovered.

Treatment.—As a preventive measure the prompt removal of the appendix once the diagnosis is assured would unquestionably diminish the percentage of cases of pylephlebitis. Of more doubtful and hypothetic value is the suggestion of Gerster that during the operation undue pressure and traction upon the structure should be avoided. As to the active treatment, there is nothing to be considered but a thorough exploration of the liver and the prompt evacuation and drainage of any abscess cavity that may be found.

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EMBOLISM.

Definition.—Embolism is the process whereby a foreign body or some undissolved material is carried by the blood and impacted in any portion of the vascular system, usually the smaller arteries and capillaries. The material so deposited is called an embolus.

Sources and Nature of Emboli.—The most common source of emboli is to be found in the vascular system, such as detached portions of thrombi from the heart or the vessels, usually the veins, which have undergone softening, fragments of heart valves, portions of atheromatous patches or diseased portions of the arteries, as in endarteritis nodosa. Emboli may consist, however, of fragments of tumors, of droplets of fat (fat embolism) or bubbles of air (air embolism), of masses of bacteria or parasites, as the filaria sanguinis hominis, or masses of hyaline material from disorganization of the blood, as in burns. Emboli may be classified as septic or toxic, and aseptic or bland.

Emboli may vary in size and shape; they may be spheric, cylindric, or flat; they may be of minute proportions or several inches in length. They vary somewhat in consistency according to the nature of the material from which they are derived; they vary in their structure generally according to whether they are observed shortly after they are deposited or whether sufficient time has elapsed to have enabled them to undergo metamorphosis. The changes which take place in the emboli and adjacent vessel walls are similar to those characteristic of thrombosis, so that in emboli of long standing it may be almost impossible to differentiate one from the other.

Seats of Embolism.—Once an embolus is set free it will be carried along by the blood-current and deposited in the terminal branches of the pulmonary or systemic arteries or the portal vein. The point of lodgment will depend upon its source. Thus emboli derived from the systemic veins will be carried into the right heart and deposited in the branches of the pulmonary artery; here they may be broken up and pass through the capillaries into the general circulation. Emboli traceable to the heart, the aorta, or its branches will be deposited at some more distant point, usually in the vessels of the kidney, spleen, and brain, less frequently in the peripheral vessels of the extremities. When the emboli come from the portal circulation, as the mesenteric vessels, they will be deposited in the liver or even in the heart and lungs. Emboli are deposited, therefore, almost invariably in the arterial or portal system. In exceptional instances, by a process known as retrograde or aberrant embolism, the emboli may lodge in the systemic veins. Apart from the source of the embolus there are certain conditions, usually of a physical nature, which determine in large measure its ultimate lodging-place. For example, emboli are deposited in the right lung oftener than the left because the right pulmonary artery is larger than the left. Emboli pass more frequently into the left common carotid and the left common iliac than the corresponding arteries on the right side because the axis of the former is more in line with the direction of the blood-current in the aorta at the point at which the vessel is given off. In addition to the size and direction of the vessel, the size of the embolus and the propelling force of the blood-current will influence the direction and course pursued by the embolus.

Results.—The effects produced by embolism will depend upon the seat and character of the embolus; they may be alarming or insignificant, transitory or permanent. Thus, air emboli obstructing the coronary, pulmonary, or cerebral artery may cause instantaneous death. The results will vary, of course, according to whether the embolus is septic or aseptic.

The immediate results of embolism are those which are due to the disturbance of the blood-supply. The embolus may entirely occlude the vessel, thus cutting off the entire blood-supply of the parts supplied by the vessel and its branches, or only partially. In the latter case a consecutive thrombosis may complete the obstruction. If a collateral circulation is established with the branches of the affected artery the embolus may do no harm. If, however, the vessel is a terminal artery, the tissues will undergo degeneration or necrosis. The latter is the regular result when the embolus is situated in branches of the splenic or renal artery, and the basal arteries of the brain, and in the central artery of the kidney and the main trunk of the superior mesenteric artery. The pathologic condition in the tissues to which an embolus gives rise is called an infarction and the section of tissue involved an infarct. If the infarct be aseptic, the tissue undergoes coagulation necrosis and is gradually absorbed and replaced by scar tissue. If the infarct be infected primarily or secondarily, gangrene, suppuration, and abscess formation will be the result. Metastatic abscesses thus formed are found most frequently in the spleen, kidney, brain, lungs, and liver.

Pulmonary Embolism after Injuries and Operation.—The relative frequency of pulmonary embolism to other forms of embolism after surgical operations, according to Robinson,[1] is as follows: "The general distribution of embolism following surgical operations is relatively: (1) pulmonary, 70 per cent.; (2) renal, 12 per cent.; (3) splenic, 8 per cent.;

(4) hepatic, 5 per cent.; (5) cerebral, 4 per cent.; (6) the serous membranes (pleura, peritoneum) and joints, 30 per cent."

As to the **frequency** of pulmonary embolism as a complication of abdominal operations, Albanus [2] found 23, or 2 per cent., in a series of 1140 laparotomies. In the surgical clinic at Munich from 1892 to 1902 there were 1196 laparotomies, of which 78, or 6.43 per cent., suffered from pulmonary complications; of these, 42 followed gastro-enterostomies, herniotomies, and gastrostomies. Of the 77 pulmonary complications, but 14, or 1.17 per cent., were secondary to embolism. Lotheissen [3] collected 66 cases of pulmonary embolism following injury or operative infarcts, including 36 fractures with 30 deaths, 6 contusions with 5 deaths, 4 tendon and muscle operations, all fatal, and 20 miscellaneous operations with 16 deaths. In this series of cases the embolus was most frequently dislodged from thrombi in the veins of the leg, in the region of the pelvis, and in the hemorrhoidal plexus.

With these general remarks, touching upon the subject more from its pathologic aspect, we will pass on now to a consideration of the symptoms and treatment of the types of embolus as they are met with in surgical practice.

As to the **origin** of the emboli, Lotheissen found in his series of 66 cases that 40 were secondary to a phlebitis and thrombosis of the veins of the lower extremity; next in frequency came those which started from thrombi in the pelvic veins in the puerperium or after operations upon the pelvic organs. In 236 operations for uterine fibroid (Burkhard[4]) there were 12 cases of embolism. Pulmonary embolism is much more common after gynecologic than after general surgical operations. It may owe its origin to the thrombi which form after the Trendelenburg operation for varicose veins, after operations upon the hemorrhoidal and pampiniform plexus, and a not infrequent cause is the thrombus complicating perityphlitis. In a series of 1000 appendectomies which Sonnenburg [5] performed in his private and public clinic there were 47 pulmonary complications. These were attributed chiefly to thrombi which formed in connection with the inflammatory process in and around the appendix. In Oppenheim's opinion thrombi are more commonly met with in perityphlitis than any other lesion, and it is a lesion therefore which may readily lead to embolism. Pietrozikowski [6] called attention to the comparative frequency of pulmonary complications in strangulated hernias. According to Gussenbauer, this is due to the fact that before the obstruction is relieved there are thrombi in the small veins of the strangulated loop, and just as soon as the strangulation is relieved the arterial circulation is restored and emboli are liberated. In the majority of operations which were complicated by pneumonia, the hernia was of the incarcerated type, and in the majority of those terminating fatally the autopsy revealed an embolic pneumonia. In the lung, as elsewhere, the obstruction of the circulation by the embolus is followed by infarction. The infarct is usually situated in the lower lobe, just beneath the pleura, and more frequently in the right side. Owing to the fact that between the pulmonary capillaries and the branches of the pleural and branchial arteries there is a free anastomosis aseptic emboli, involving only the smaller branches of the pulmonary artery, do not give rise to any structural changes in the parenchyma, and therefore there may be no symptoms. When, however, there is already some circulatory disturbance, as a passive venous congestion, the conditions are more favorable for the development of an infarct. In the lung, therefore, the infarcts are almost invariably hemorrhagic. Hemorrhagic infarction is usually ushered in with a chill or chilly sensation and a rise of temperature. Fever, however, is not a conspicuous symptom; the temperature may return to normal within twenty-four hours or remain elevated for some days. The patient often complains of pain in the side and of a sense of constriction across the chest. An examination of the chest the day after the infarction may reveal the signs of consolidation and of an associated sero-fibrinous pleurisy.

The most characteristic **symptom** of pulmonary infarction is hemoptysis; the expectoration of blood-stained sputum, at first dark red, but later becoming brownish-red, should always arouse one's suspicion.

The **diagnosis** of pulmonary infarction is not always easy; in some cases it may be impossible to elicit any physical signs, and the hemoptysis and other phenomena are by no means constant.

When the embolus or emboli are of such dimensions as to occlude the larger branches of the pulmonary artery, death may be almost instantaneous. Robinson[1] related his experience with a case in which he was examining a patient upon whom he had performed a hysterectomy seventeen days before; upon flexing the thigh the patient screamed with pain, struggled for breath, became more and more cyanotic, and died in forty-seven minutes. The autopsy revealed an aggregation of emboli in the pulmonary vein which had come from a thrombophlebitic ovarian vein. The sudden appearance of symptoms indicative of respiratory distress in a patient who has recently submitted to an operation, especially upon the pelvic organs, appendix, or the bowel in strangulated hernia, should at once suggest at least pulmonary embolism.

The **prognosis** of pulmonary embolism is very variable and depends altogether upon the size of the vessel involved. In the case of the large vessels the condition is almost invariably fatal; death is often instantaneous. In embolism of the smaller vessels associated with hemorrhagic infarction the prognosis is favorable if the lungs were previously healthy.

The **treatment** of pulmonary embolism consists essentially in rest, together with the administration of strychnin, oxygen, and morphin. In very large emboli particularly nothing can be done to relieve the asphyxia from which the patient dies. Treatment is of so little avail that every precaution should be taken which is regarded as prophylactic. Absolute rest should be enforced whenever thrombosis is known to exist or even suspected. A sudden and otherwise unaccountable increase in the pulse during the convalescence from an operation should at least suggest thrombosis. After the loss of a large amount of blood an artificial anemia should be guarded by the free administration of saline solutions. When a post-operative thrombosis develops in the veins of the extremity, the patient should be kept absolutely quiet for a period of four to six weeks;

that is, until the thrombus has become fully organized. Early operation upon strangulated hernia and for appendicitis must be regarded as a prophylactic measure when one takes into consideration the relative frequency with which pulmonary embolism follows these conditions. The longer the delay, the greater the time allowed for thrombus formation.

So much as has been said applies to the bland or aseptic type of embolism. When the source of the embolus is an old septic thrombosis, a local suppurative process, as an acute osteomyelitis or a malignant endocarditis, the resulting lesions may be at first an anemia or hemorrhagic infarct, but subsequently the organisms invade the surrounding tissues. The infarcts become infiltrated with leukocytes, the tissues undergo liquefaction, and small irregular cavities are formed which are called metastatic abscesses. On account of the proximity of these lesions to the pleural cavity the pleuræ become involved in the inflammatory process and a purulent or fibrinopurulent pleurisy develops. The peribronchial and intralobular lymph-vessels may be filled with a purulent exudate, and under some circumstances the interlobular connective tissue is invaded. The metastatic abscesses may rupture into the bronchi or into the pleural cavity. Occasionally recovery may take place by absorption.

The symptoms of septic embolic pneumonia are those of pyemia. The prognosis is grave; the treatment is chiefly supportive. When there are reasons to believe that a large abscess has formed from the coalescence of smaller ones, surgical interference should be seriously considered.

Embolism of the Mesenteric Artery.—The results of circulatory disturbances of the mesenteric vessels have been so fully discussed under the section on thrombosis that but little remains to be said as to embolism. The source of the embolism differs in no particular from that involving other vessels, and includes such lesions as thrombophlebitis, septic processes, as in pyemia and septicemia, endocarditis, vegetations of the cardiac valves, and arteriosclerosis. In the majority of cases the embolus is situated in the superior mesenteric rather than the inferior mesenteric artery. Inasmuch as the superior mesenteric is a terminal artery, the results following its obstruction are very much more serious than those that follow an embolism of the inferior mesenteric artery. In an obstruction of the inferior mesenteric artery a collateral circulation may be established through the branches of the middle and inferior hemorrhoidal and the superior mesenteric arteries; the resulting lesion is almost always a hemorrhagic infarct involving a variable portion of the small intestine. If the main artery itself or one of its larger branches is the seat of obstruction, a considerable portion of the intestine may become gangrenous. The smaller the branch involved, the smaller will be the infarct. In exceptional cases the resulting lesion will be an anemic rather than a hemorrhagic infarct.

The **symptoms** are practically those which have been described as common to thrombosis; sudden colicky pain, diarrhea, and unaccountable and sometimes profuse hemorrhage, paralysis of the intestine, and rapidly developing ileus. If the gangrenous section is not removed by operative measures, perforation and peritonitis will inevitably follow.

The **prognosis** of embolism is always most unfavorable; the symptoms develop so rapidly and the nature of the lesion is sometimes so obscure that the patient may be moribund before the diagnosis has been established or operative intervention considered.

The positive **diagnosis** is often impossible, although the presence of profuse hemorrhage associated with sudden colicky pain, distention, and signs of obstruction not accounted for in any other way should at once arouse one's suspicion as to the existence of a mesenteric embolism.

Treatment.—Spontaneous recovery is so exceptional and the dangers of delay so great that an exploratory operation should be performed at the earliest possible moment. The only chance of the patient's recovery lies in a resection of the affected bowel, and even after the abdomen has been opened it is difficult to determine how much of the bowel is likely to become gangrenous and should therefore be removed. Owing to this uncertainty Porter [7] advises that the involved gut should be brought well out of the wound, allowing liberal sound margins at either end. After resecting the visibly gangrenous portion of the bowel the open end should be fixed in the wound and the region well walled off with gauze tampons. Thus the distention is relieved and the intestine can be kept under observation for the further development of gangrene.

Embolism of the Renal Artery.—Embolism of the renal artery of the bland variety is usually of the anemic type, although in exceptional instances true hemorrhagic infarcts may occur. In either case they are of no practical significance from a surgical point of view. Septic or infective emboli are capillary in size and give rise to the hematogenous form of suppurative nephritis. Inasmuch as the kidney is an organ of elimination, it is not surprising that this organ should frequently become involved when there are septic processes in other parts of the body. At the points at which the emboli lodge the bacteria grow and even spread to the surrounding tissue, where they excite an inflammatory process; at first a hyperemia with a rapid infiltration of leukocytes and later liquefaction necrosis, and the formation of an abscess. These embolic or metastatic abscesses appear to the naked eye as red, gray, or yellow spots or streaks. The smaller abscesses coalesce and give rise to larger ones, and if the patient live long enough the entire parenchyma may be riddled with abscess cavities of variable size. This complication is ushered in with a chill and rapid rise of temperature, followed by hematuria, pyuria, albuminuria, and oftentimes suppression of urine. As both kidneys are usually involved, the prognosis is absolutely unfavorable.

Embolism of the Peripheral Vessels.—Embolism of the peripheral vessels is by no means as common as thrombosis. That is to say, thrombosis of the peripheral vessels usually involves the veins and is not of embolic origin. Peripheral embolism, on the other hand, is essentially a disease of the arteries. Comparatively speaking, peripheral embolism is not very common; thus of a series of cases cited by Ziemssen,[8] in 84 cases of embolism the kidneys were affected 57 times, spleen 39, the liver and alimentary canal 5, and the skin 14; no clots in the larger arteries of the extremities were reported. According to Ziemssen, embolism of the larger arteries of the extremities is of rare occurrence, and of these the commonest cause is valvular disease of the heart. The most common predisposing causes of arterial thrombosis of the extremities are endocarditis and the infectious diseases, especially typhoid fever, pneumonia, influenza, and enteric fever. When secondary to endocarditis the vessels of the upper extremity may be involved as frequently as those of the lower extremity. As examples of embolism of the upper extremity may be cited the cases of Martindale,[9] Davidson,[10] and Sherwood,[11] involving respectively the radial, brachial, and axillary arteries. Though arterial thrombosis is by no means an uncommon complication or sequel of the infective diseases, those cases originating in emboli are decidedly in the minority. The emboli are usually of cardiac origin, although they may come from thrombi which have formed in the vessels between the heart and the extremities. Gibson,[12] who reported three cases of gangrene complicating pneumonia, believes the cases were directly due to the pneumonic condition and not to some intercurrent or accidental process. The emboli come from the fibrinous masses which are seen in the pulmonary capillaries or larger vessels in the hepatized area. From 1895 to the time his report was made in 1903 he was unable to find any other cases reported in literature. This condition must be more common than it would appear from this statement, since I have seen in consultation two cases within the past few years. As to typhoid fever, Keen [13] points out that the extraordinarily even distribution on the right and left sides in cases of arterial obstruction as contrasted with venous obstruction would seem to suggest the cause to be much more frequently embolic than has been hitherto believed. Of 61 cases, 12 were bilateral, 25 on the right, and 24 on the left side. It might be said, further, in favor of the embolic origin that a large percentage of the cases (18 out of 41) occurred during the second or third weeks; that is, during the period of greatest cardiac weakness. The lower extremity is involved much more frequently than the upper extremity; of 128 cases of thrombosis, only 5 involved the upper extremity alone and two the upper and lower extremity.

The **symptoms** of arterial embolism are those of a sudden interruption of the blood-current. Without any warning the patient is suddenly seized with a sharp pain in the affected limb, referred often to the seat of obstruction. The extremity below the seat of the obstruction becomes cold, numb, livid, and edematous; there is no pulsation in the vessels below the seat of obstruction. The subsequent phenomena will depend upon whether or not the point of obstruction will admit of the establishment of a collateral circulation. If the latter is possible, the symptoms gradually subside, the temperature returns to normal, sensation returns, the edema disappears, and pulsation may again be felt in the distal vessels. The chances for restoration of a collateral circulation are greater in the upper than in the lower extremities. If the circulation through the collateral branches is not restored, gangrene of the dry variety will follow.

The **diagnosis** between arterial embolism and thrombosis may be a matter of some difficulty or even impossible. If the embolus at first only partially occludes the vessel, the symptoms may simulate thrombosis; and if the thrombosis is of exceedingly rapid formation, the symptoms may simulate embolism. Generally speaking, the sudden onset, the sharp pain, the absence of arterial disease, the association of an endocarditis, especially in children and young adults, point to embolism, whereas the gradual disturbance of the circulation and preëxisting disease bespeak a thrombosis.

The **treatment** of this embolic gangrene depends somewhat upon circumstances. The principles involved are more appropriately considered in the chapter on Gangrene. Suffice it to say that, as a rule, it is wiser to defer amputation until the line of demarcation has formed. In deciding this question the surgeon should be influenced principally by the condition of the patient.

Embolism Following Paraffin Injections.—Since 1900, when the Viennese surgeon Gersuny recommended for the correction of deformities of the nose subcutaneous injections of melted paraffin, another has been added to the list of possible causes of embolism. While this method of treatment has proved so satisfactory from the cosmetic point of view, there is this one objection to it, namely, that fatal embolism has followed its use in some instances. Both Pfannenstiel and Halban[14] reported a case of pulmonary embolism following paraffin injection at the neck of the bladder. This accident has been attributed by Gersuny to the employment of paraffin with too high a melting-point, while by others the accident has been believed to have resulted by the direct injection of the paraffin into the vein. It would seem reasonable to suppose that the lower the melting-point of the paraffin, the greater the danger of embolism, since the longer it remains liquid after its injection into the tissues. It is a better plan, therefore, if using paraffin at all, to select that which has a high melting-point. In its application to the deformities of the nose a further precaution may be taken by making direct pressure over the tissues at the root of the nose in order to prevent, at least at the time of injection, if possible, the passage of the paraffin into the general circulation.

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AIR EMBOLISM.

Historical.—In 1683 Heyden observed that when air was injected into the crural vein of a dog the fluid reached the heart instantly, the animal went into convulsions, and the heart's action was arrested. Both Hardel and Brunner (1684) injected air into the external jugular vein of a dog, observed the fatal effect, and found frothy blood in the heart. That the forcible injection of air into the veins of animals would cause death was known also to a number of other observers, as Morgagni (1760), Haller (1757), Tissot (1784), and Postal (1800). The first observation of the spontaneous entrance of air into the veins was made by Terrier in 1806, in the case of a horse who had sustained a wound of the vessels of the neck. The first authentic record of this accident in man was observed by Beauchène in 1818 and reported by Magendie in 1821; the accident occurred during an operation for the removal of a tumor necessitating an excision of the clavicle. Three years later Dupuytren reported the second case, and the autopsy revealed a considerable amount of air in the vessels and right auricle. From that time on the observations become more frequent, and in the early part of the nineteenth century a number of experiments were made with a view toward throwing some light upon the pathogenesis, chief among which was the well-known work of Amussat.[1] The latter in 1839 collected 32 cases: of these, 9 were confirmed by autopsy, 6 were unquestionably cases of air embolism but were not confirmed by autopsy, 5 were doubtful, and the remainder were followed by recovery.

Clinical Phenomena.—It has already been said that air embolism is regarded as a possible cause of sudden death. The accident most frequently occurs during operations or after accidents in the so-called danger zone, but many cases have been reported in which the air gained entrance to veins more or less distant. A fatal amount of air may be introduced into the veins in venesection or in intravenous injection of a saline solution. A case was reported by Jurgensen[2] in which death was attributed to the entrance of air into an open vein in a gastric ulcer, and Janeway[3] suggested that the cerebral phenomena, which have been occasionally observed after irrigating the pleural cavity with hydrogen peroxid, have been due to the air embolism of the cerebral vessel. The symptoms and death in caisson-disease have been attributed to the liberation of nitrogen in the circulating blood, following the rapid reduction in the atmospheric pressure upon exit from a caisson. These manifestations of air embolism are some of them questionable, and exceptional as compared with those following the opening of a vein in accidents or operations.

There are various reasons, both physiologic and anatomic, why this accident should happen most frequently in the veins at the base of the neck. In the first place, there is in these veins during inspiration a negative pressure, and should the vein be wounded and not collapse, more or less air will be sucked in with each inspiratory act. In a series of observations upon sheep Jacobson[4] prepared the following tables comparing the pressure in veins in close proximity to and more or less distant from the heart:

In the left vena anonyma	— 0.1	mm. Hg.
“ “ right “ jugularis	+ 0.2	“ “
“ “ right “ subclavia	— 0.1	“ “
“ “ left “ jugularis	— 0.1	“ “
“ “ left “ subclavia	— 0.6	“ “

In the external facial	+ 3.0	mm. Hg.
“ “ internal “	+ 5.2	“ “
“ “ brachial	+ 4.1	“ “
“ a branch of the same	+ 9.0	“ “
“ the crural vein	+11.4	“ “

This aspirating effect of the respiration is only operative a short distance from the heart, as far as the jugular and the axillary veins (as can readily be seen in operations in these regions), and to this region the term "danger zone" has been appropriately applied. As a result of a series of experiments made upon dogs by a commission appointed by the Royal Academy of Medicine of Paris, it was claimed that the wound in the vein must be within the area of the venous pulse or not far from it. As to the extent of the venous pulse it was determined by the commission that the brachial and axillary veins were beyond and the subclavian and lower third of the jugular veins were within the venous wave. Many cases have been recorded, however, to demonstrate that this accident has occurred outside the area of venous pulse and that it always occurs during inspiration (Senn[5]). The anatomic conditions which predispose to the entrance of air into the veins are the peculiar relation of the external jugular vein to the cervical fascia and of the axillary vein to the costo-coracoid membrane. The unyielding nature of these layers of fascia prevents the walls of the veins from collapsing when they are wounded.

In fact, any condition which prevents the wall of the vein from collapsing is likewise a predisposing factor, as, for example, inflammatory lesions of the veins, calcification of the venous walls, adhesion of the vein to surrounding structures, as tuberculous or malignant lymph nodes. Apart from these conditions, some anatomic, some physiologic, and some pathologic, it has been said that the posture of the patient is a factor which must be taken into consideration. Thus, according to Goodridge,[6] the entrance of air into the veins is favored by the semi-prone or sitting posture, and the elevated position of the pelvis during operations upon the uterus is believed to favor the entrance of air into the uterine veins.

The preponderance of cases which result from injuries to veins in the neighborhood of the heart is illustrated by the series of cases collected by Couty.[7] Of 33 cases, the point of entrance was in the external jugular nine times, in the axillary eight times, in the internal jugular five times, in the subscapular three times, in the facial, occipital, anterior jugular, and anterior thoracic, each twice. This accident occurs with the greatest frequency after operations for the removal of tumors from the neck and axilla, after shoulder-joint amputations, ligation of the subclavian, resection of the scapula. That the accident may occur when the vein injured is at a considerable distance from the body is illustrated by the following cases. The first was the only well-authenticated case of aspiration of air into the femoral vein which Senn was able to find. Three and one-half days after an amputation of the thigh, the patient died suddenly without any obvious cause. At the necropsy it was found that the right cavities of the heart, the two iliac veins, and the inferior vena cava were distended with a mixture of blood and air. The autopsy in this case was not made until twelve hours after death, and inasmuch as the surfaces of the flaps in the stump were separated by gaseous products, it is more than probable that the air which was found in the heart and vessels was not the atmospheric air, but gas which had developed in the wound. Warren[8] reported a case in which a distinct sucking sound was heard when the internal saphenous vein was wounded in removal of a tumor from the thigh.

Cranial Sinuses.—In addition to the veins of the neck, thorax, and extremities, fatal cases of air embolism have been reported in connection with the cranial sinuses. Genzmer[9] reported a case in which Volkmann operated for the removal of a sarcoma of the dura mater. During the course of the operation on dividing the falx cerebri there was a tremendous hemorrhage, and the sound characteristic of air embolism was heard. A sponge was immediately applied to the wounded sinus, and after a short interval the operation was resumed. Upon attempting to divide the posterior attachment of the tumor to the longitudinal sinus air again entered, and the patient went into collapse and died a few moments later. Bergmann (quoted by Goodridge) described a case of a man who died four hours after receiving a blow upon the occiput. At the autopsy every evidence of air embolism was found, and it was assumed that the air had entered through the injured torcular.

A number of experiments have been conducted to observe the effects of the aspiration of air into the superoir longitudinal sinus, notably by Genzmer[9] and Senn.[5] The results of these experiments were only confirmative of what has been observed clinically. There are certain conditions peculiar to the cranial sinuses which would seem to favor the aspiration of air. In the first place, the elevated position of the head plays no inconsiderable part. This is the position in which the head is placed, as a rule, during operations, and the one which is regarded as an influential factor. The rigidity of the sinus walls and their attachment to the bony structures are such as to prevent the sinus collapsing after it is wounded. Another predisposing factor, the influence of which has been proved by experimentation, is hemorrhage. The influence of severe hemorrhage upon the aspiration of air into the veins is a very positive one, and the wound of a cranial sinus is always attended by profuse and alarming hemorrhage. To sum up, therefore, we have in the cranial sinuses conditions which are most favorable for the entrance of air through an accidental wound, namely, the profuse hemorrhage, the rigidity of the sinus walls, and the customary elevation of the head during operations.

Uterine Veins.—There are certain conditions peculiar to the uterine veins which favor the aspiration of air; as a complication of labor or gynecologic operations. During pregnancy the uterine veins become enormously dilated, and when the placenta is detached some of the sinuses may be exposed. If the uterus contracts and remains firmly contracted after delivery, the danger of air embolism is reduced to a minimum; but if the uterus after contraction becomes relaxed and the uterine cavity contains air, the latter will be drawn into the sinus by suction, as the uterine muscle relaxes, and may be forced into the circulation when the uterine muscle again contracts. Attention was first called to the danger of air embolism after parturition by Legallois in 1829, and Cormack in 1850 described 3 cases which had occurred in his neighborhood (quoted by Senn). Since that time a number of other cases have been reported, and a number of fatal cases were collected by Perkins.[10] As to the causes of air embolism during gynecologic operations, not the least important is the Trendelenburg position. Reference has been made already to the effect of posture upon the aspiration of air into the cranial sinuses, and inasmuch as so many operations upon the pelvic organs are conducted with the patient in the Trendelenburg position, we have an almost constant and predisposing cause for the occurrence of this accident. A second factor is the anemia which is so common a symptom of uterine carcinoma and fibroid. We refer here not to the anemia attending hemorrhage during operations, but that which has developed as a result of the cancerous cachexia, or the more persistent uterine hemorrhages. The third predisposing cause is the dilated condition of the veins, particularly those of the broad ligament, which is so frequently found in association with uterine fibroids. An interesting discussion of this condition appears in the article of Delore [11] in which he reports a fatal case of air embolism following an abdominal panhysterectomy for the removal of a uterine fibroid. One must accept with much skepticism the explanation of sudden death following injections into the uterus, usually for the purpose of committing a criminal abortion. While some of these may be due to the entrance of atmospheric air into the uterine sinuses, some cases so reported have been found to be the result of the invasion of the Bacillus aërogenes capsulatus.

Symptomatology.—The clinical picture produced by the entrance of air into veins is quite characteristic and more or less uniform. Usually, but not invariably, a peculiar sound, described as sucking, gurgling, or hissing, is heard. This sound may be scarcely audible, or loud enough to be heard at a distance, and is usually attended with the appearance of bubbles of air in the wound. If the patient is conscious and not under the influence of an anesthetic, he not infrequently utters a cry of anguish, as in the classic case of Beauchêne, described by Magendie,[12] in which the patient suddenly cried out: "My blood is leaving my body! I am dead!" Then follow the symptoms of collapse, the face becomes pale and livid, the pupils dilated, and the reflexes abolished. Probably as a result of the embarrassment of the pulmonary circulation, there is marked disturbance of the respiratory act. The respirations become irregular, accelerated, deep, and labored. These respiratory difficulties are quite a conspicuous feature not only in human subjects but in animals in which this condition has been brought about for experimental purposes. As to the cardiac phenomena, the heart becomes weak and irregular, the pulse accelerated and scarcely perceptible, and a churning systolic sound, due to the presence of air within the heart cavities, may be heard upon auscultation; finally, in those cases not under the influence of a general anesthetic convulsive seizures, more or less general and violent, may develop.

The Immediate Cause of Death after Air Embolism.—It may be said by way of preface that by the term "air embolism" is indicated a condition which is due to the entrance into the venous circulation of a quantity of atmospheric air. Attention was called to the presence of spontaneously generated gas in the tissues and blood after death many years ago, but it was not until 1891 that a systematic bacteriologic investigation was made to determine the nature of the gas bubbles, which resulted in the discovery by Nuttall of an anaërobic bacillus, the Bacillus aërogenes capsulatus. The mere finding of bubbles of gas in the heart and blood-vessels after a sudden and unaccountable death cannot, therefore, be accepted as indicating that the patient died of air embolism. In all doubtful cases, that is, in cases in which there was no positive evidence that air entered the vein during an operation and the patient did not exhibit the characteristic symptoms, a careful bacteriologic examination should be made to determine the presence or absence of gas-producing organisms. The study of the effects of the introduction of air into veins has been a most engrossing one. Chapters could be written if one attempted to review all the experimental work, which has been carried on from the seventeenth century to the present day upon this subject alone. The results of these experiments have been in many respects uniform. It has been determined that in some cases a large quantity of air may be introduced into the vein of a dog without any apparent ill effect. In others, again, a similar quantity will produce the symptoms observed in man, to be followed in some cases by recovery and in some by death. It has been proved that the effect is influenced by the manner in which the air is introduced. If the air is introduced slowly, there is less likelihood of a fatal issue. Laborde and Muron [13] injected 1120 c.c. into the vein of a dog in the course of an hour and a half without producing any apparent effect. Although the dog and the horse appear to be so much more tolerant of the presence of air in the circulation than the human subject, experimental investigation has been interpreted as proving that air embolism is in man a possible cause of death. This was once a much mooted question, and even such distinguished surgeons as Velpeau and Fergusson doubted that a sufficient quantity of air could be admitted through a wounded vein to cause death. That there was still some doubt even in comparatively recent times as to whether air embolism could be regarded as a possible cause of sudden death, may be gathered from the conclusion at which Hare [14] arrived at the termination of a carefully conducted series of experiments. "(1) Death never occurs from the entrance of air into the ordinary veins of the body unless the quantity be enormous; from one to several pints, a quantity which cannot enter unless deliberately sent in by the surgeon. (2) The cases on record have been due to other causes than air and have not been proved. (3) The tendency of the vessel to collapse and the leakage of blood prevent any entrance of air, and it would seem probable that a clot has generally caused death, not the air itself."

While air embolism is admitted as capable of causing death, it is generally known that the entrance of air into the veins is not necessarily a fatal accident. That is to say, there have been cases in which a small amount of air has entered the vein either without producing any effect whatsoever, or if some disturbance arose, without a fatal termination.

There have been endless disputes and discussions as to the actual cause of death. Upon examination of the tissues after death the right ventricle and auricle have been found distended with frothy blood, air-bubbles have been found in the blood of the veins, especially those near the heart, numerous air emboli have been seen in the pulmonary capillaries, and the left auricle and ventricle are usually empty—only exceptionally is the air forced through those pulmonary capillaries to enter the general circulation. There may be said to be three theories advanced to account for death—the cerebral, the pulmonary, and the cardiac.

Cerebral Theory.—Morgagni was the first to attribute the fatal termination to the disturbance of the cerebral circulation. He believed the air-bubbles, when lodged in the small veins, caused them to distend and thereby exert pressure upon the nerve centers. Bichat (*loc. cit.*) believed the brain was the first to suffer, and attributed death to a cerebral anemia produced by the presence of air in the cerebral vessels. Senn (*loc. cit.*) sums up the arguments which he advanced as follows: "As the first argument in favor of this view, he claims that the heart continues to beat for some time after the cessation of animal life. Secondly, air injected through one of the carotids produces death in the same way as when introduced into the veins. Thirdly, the cases reported by Morgagni, where death was attributed to the presence of air which was found in the cerebral vessels at the post-mortem examination, and which was supposed to have developed there spontaneously. Fourthly, all examinations after death revealed the presence of frothy blood, mixed with air-bubbles, in both ventricles. Fifthly, air injected into one of the divisions of the portal vein produces no ill effects until it reaches the general circulation. Sixthly, the almost instantaneous death observed in some instances is due to the acceleration of the heart's action, and consequently the rapid conveyance of air into the cerebral vessels. Seventhly, the existence of convulsions, which he ascribes to the irritating quality of the air on the brain."

There may be said to be some doubt as to whether the air emboli can pass through the pulmonary capillaries and gain entrance into the general circulation at least in the human subject. If such a phenomenon is possible, it is the exception rather than the rule. We cannot look upon any condition of the brain as playing a primary and essential rôle in the causation of death after air embolism in the majority of cases. The cerebral anemia, which, however, is only secondary to the cardiac embarrassment, may be held accountable at least as a contributory factor in some fatal cases.

Pulmonary Theory.—There is little doubt that the presence of air in the pulmonary circulation has a deleterious effect by embarrassing the action of the heart, but not to the extent of causing cardiac failure. According to Piédagnel [15] and others, when air-bubbles enter the lungs, the air expands, ruptures the capillary walls and escapes, producing an emphysema. The pressure of the escaping air upon the pulmonary capillaries in the neighborhood seriously interferes with the pulmonary circulation. This hypothesis is scarcely sustained by the experience of Couty, who in 28 autopsies did not see one case with emphysema. Another group of observers, represented by Boerhaave, maintained that the air-bubbles did not break through the capillaries, but lodged there and produced a fatal pulmonary embolism. These views were based largely upon the results of laboratory experiments, in which small glass tubes were used to represent the capillaries. Nysten [16] is quoted as never having found air in the arterial system; both Nicaise [17] and Hauer [18] concluded from their experiments that air-bubbles could not penetrate the capillary walls. The former based his opinions upon the observations of Jamin, who found that it required a great amount of pressure to force a column of water mixed with bubbles through a column of mercury in a very small capillary tube of glass. As Delore points out, experiments are not convincing, since it is not fair to compare the elastic expansile capillaries of the lung with an unyielding glass tube. The fact that, as in so many cases, the left side of the heart is empty would seem to prove that the blood cannot pass through the pulmonary capillaries.

Cardiac Theory.—We come now to the third and most important of the three theories. Some of the older writers maintained that the heart's action was arrested by the toxic action of the carbonic acid contained in the air, but Roux and Delpech[19] made an analysis of the air and found that it contained no carbonic acid; furthermore, Nysten injected large quantities of CO_2 into the veins without causing death. It was even claimed that the interference with the heart's action was the result of the sedative action of air, but this view is contrary to the experience of physiologists, who claim that air has a stimulating rather than a depressant effect. Magendie, Bouillaud, and later Couty [1] attributed the circulatory disturbance to the accumulation of air in the right heart. When air accumulated in sufficient quantities the heart became distended and the valves could not close. The inability of the ventricle to force the mixture of air and blood into the circulation is due to the compressibility of the air. The insufficiency of the tricuspid valves has been held accountable for the venous pulse which is a constant symptom in all cases which prove rapidly fatal. According to Franck,[20] the ill effects of air embolism are due not only to tricuspid insufficiency, but to cerebral anemia, and to obstruction of the coronary vessels. When a quantity of air is introduced into the veins it accumulates in the right auricle and right ventricle, mixes with the blood, part is forced into the pulmonary vessels, and part regurgitates into the veins. As a result of the inability of the tricuspid valves to close, the frothy blood is forced back through the veins into the brain and causes the cerebral phenomena described by Couty. At the same time there is a reflux of frothy blood into the coronary veins; this obstruction of the coronary circulation must exert a paralyzing influence upon the action of the heart. It has been said that the sudden deaths which take place in diastole are the result of the sudden distention of the ventricle caused by the increase in volume of the air when subjected to the higher body-temperature.

These are the various theories, some of them more or less speculative, which have been advanced from time to time to account for the fatal termination of air embolism. It is not possible to single out any one of these three as primarily responsible in all cases, so that we must be content to acknowledge that each one of them may play some part in the sequence of events. From the experimental and clinical evidence one is justified in regarding the cardiac disturbance as the most important primary factor. In the tricuspid insufficiency, in the sudden distention of the ventricle, and the obstruction to the coronary vessels there is enough to account for the serious or fatal embarrassment of the heart's action. There are some cases in which the heart continues to beat after the arrest of the respiratory function; in such instances death is due to suffocation as a result of pulmonary embolism or to cerebral anemia. Treves[21] believed that death was due to the arrest of the pulmonary circulation, Hare[14] to primary respiratory failure, and Goodridge[22] to secondary respiratory failure, resulting from brain anemia. In the face of this conflicting evidence we are forced to conclude that the immediate cause of death may be either tricuspid insufficiency and obstruction of the coronary vessels, pulmonary embolism, or cerebral anemia.

Diagnosis.—The ante-mortem diagnosis should not be a matter of great difficulty, although there must always be a certain amount of doubt attending the diagnosis unless it has been confirmed by subsequent autopsy, and the same is true of those cases in which patients are said to have recovered. The accuracy of these reports has not been regarded as indisputable. Although, as it has been said, a positive diagnosis can only be made by the autopsy findings, a preliminary diagnosis may be based upon the following symptoms: the respiratory embarrassment, convulsions, the feeble and irregular pulse and the peculiar bruit heard upon auscultation, the characteristic sound heard upon the entrance of the air into the vein, and the reflux of blood mixed with air into the vein, and the reflux of blood mixed with air from the injured vein during systole. With reference to the necropsy, the possibility of the gas, found in the vessels and heart post-mortem, having been generated by the gas-producing organisms should not be lost sight of.

Treatment.—Inasmuch as the entrance of a small quantity of air may lead to a fatal issue, despite in many cases the adoption of the most radical treatment, it is all-important that every means should be adopted to prevent the occurrence of this accident. It is proper, therefore, to speak first of the prophylactic treatment. In operations for the removal of malignant growths in the so-called dangerous zone, Langenbeck suggested that the vein on the proximal side of the tumor should be exposed before attempting its removal, so that in case the vein was wounded direct compression might be made on the proximal side of the opening. In specially dangerous cases it might be advisable to apply a temporary ligature or artery clamp to the vessel at this point before undertaking to remove the growth. Before dividing a vein in the course of a dissection, hemostatic forceps should always be applied.

The active treatment of air embolism consists in the prevention of the ingress of an additional amount of air, in the administration of certain remedies to sustain the action of the heart and prevent collapse, and in the adoption of certain measures to relieve the embarrassed right heart. The treatment must in every case be energetically and rapidly applied, inasmuch as in many instances a few minutes will elapse before the patient succumbs. Immediately after the accident is observed the surgeon should at once make direct compression over the vein with a compress, or preferably with his finger, and at the same time the wound may be filled by an assistant with salt solution. This will prevent an additional quantity of air from entering the vein, and may save the patient's life. To sustain the action of the heart cardiac stimulants should be administered hypodermatically, and of these nitrate of amyl is the most efficient remedy because of its rapidity of action and of its effect upon the blood-vessels. By automatically dilating the blood-vessels the intravascular pressure is diminished and the strain upon the heart somewhat relieved. In addition to nitrate of amyl, it might be well to administer hypodermatically such general stimulants as strychnin, camphor, and alcohol. It has been proved quite conclusively not only by necropsy findings, but by experimental investigation, that the over-distention of the right ventricle is the factor which is responsible for the fatal issue in the majority of cases. A number of experiments have been conducted to determine the feasibility of relieving this condition by puncture of the right ventricle combined, as Senn recommends, with catheterization of the right auricle. He practised this method in his animal experimentation in seven instances, with the result that three of the animals recovered and four died. The amount of air injected into the subjects, he said, was sufficient to destroy life, so that it could be safely assumed that the animals would have died but for this speedy resort to aspiration and catheterization. Puncture of the ventricle should not necessarily be practised in every case, but only in those in which there is such evidence of paralysis of the right ventricle as might be indicated by collapse and suspension of the heart's action. The needle is introduced in an oblique direction from below upward in the left intercostal space about 1½ inches from the margin of the sternum between the fourth and fifth ribs. It should be slowly advanced until the spumous blood is seen to escape and should be allowed to remain until the blood is no longer mixed with air. Delore and Duteil suggest that the needle be introduced into the right auricle rather than the right ventricle, and selected for this purpose a point 1.5 cm. from the left border of the sternum in the third intercostal space. These authors practised this method upon a patient suffering from the effects of air embolism, but too late, as they believe, to have had any beneficial effect. They succeeded in recovering a considerable quantity of spumous blood, but not soon enough to save the patient's life. This is, I believe, the only case in which this operation has been practised on the human subject for the relief of this condition, although it is an operation which has proved successful in the relief of the distended right heart accompanying acute edema of the lungs. Wisbrock, Levy, and Dana (quoted by Delore) have used this method successfully under such conditions. Goodridge advises that the spumous blood should be replaced with an equal amount of normal salt solution at a temperature of 115° to 120° F. As a result of both clinical experience and experimental research it would seem that puncture of either the right ventricle or auricle was a perfectly justifiable procedure, and should be practised in every case in which there are indications of embarrassment of the right heart. Senn would go still further in cases in which the accident occurred to a vein in the neck and introduce a Nélaton catheter directly into the auricle. He admits, however, that there is a certain amount of danger attending this operation, namely, that the presence of a foreign body such as a catheter may excite the formation of a thrombus. This danger, taken into consideration with the risk of an additional amount of air entering the vein during the process of catheterization, is sufficient to condemn this procedure. The advisability of practising venesection is also considered by Senn for the purpose of still further relieving the embarrassment of the right heart. In order to economize time the bleeding should always be done, if practicable, from the distal end of the wounded vein.

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FAT EMBOLISM.

Historical.—Magendie[1] appears to have been the first to recognize the fact that fluid fat might cause obstruction of the vessels, and the first to study the effect of fat embolism experimentally. Although unfamiliar with the manifestations of fat embolism in man, he described the symptoms accompanying it with remarkable accuracy. Later on Weber[2] and Schwick[3] conducted a series of experiments, by which it was proved that the introduction of certain emulsions into the circulation was not followed by embolism. Virchow[4] injected oil into the veins of the neck of a dog; the animal died and the autopsy revealed an acute edema of the lung and the presence of fat in the small capillaries of the lung and kidney. The first observations of fat embolism in the human subject are accredited to Muller[5] and Cohn. These observers did not attach any importance to their findings but regarded them in the light of curiosities. Zenker[6] was the first to observe fat emboli in the pulmonary capillaries in man; the patient had sustained a fracture of several ribs and an extensive rupture of the liver. From this time the question excited the interest of a number of men, including von Bergmann,[7] Hohlbeck,[8] and Schwick.[3] The most comprehensive article containing a complete review of the clinical and experimental evidence bearing upon the subject of clinical evidence was contributed by Schriba.[9]

Clinical Manifestations.—This accident has been recorded as complicating fractures, injuries of the panniculus adiposus attending severe contusions, hemorrhage into or rupture of the liver, acute inflammatory diseases of the bones, and forcible straightening of partially ankylosed joints. It goes without saying that it occurs only when the lesion is situated in tissues containing an abundance of fat, such as the medulla of bone, the liver, the subcutaneous tissues, when a vessel wall has been ruptured and when there is sufficient force to propel the fat into the vessel. Because the medulla of bone contains but little fat at that time of life, fat embolism does not occur in children.

Meet[10] collected 113 published cases of fracture in which death was attributed to fat embolism. Upon closer examination he concluded that of this entire series there were but eleven cases in which it could be said with any degree of certainty that death was directly attributable to fat embolism; added to these were two which came under his own observation. This number is relatively small when one takes into consideration the frequency of this accident and the fact that fat embolism in all probability accompanies every fracture, so that in the majority of cases it is entirely innocuous. Schriba (*loc. cit.*) examined the urine in 24 cases of fracture and found fat emboli 22 times, and the reports of others are equally positive. The majority of cases occurred during the third decade of life, a period in which fractures are most frequent. In every case the fracture was situated in the long bones and in most instances more than one bone was involved. In 13 cases the bones of the lower extremity were involved exclusively; the femur was involved ten times, the tibia eleven, and the fibula three. In this series of cases the majority proved fatal within three days, one died in three hours, and four survived four, eight, ten, and eleven days respectively.

Though the greatest number of fatal cases have been associated with fractures, fat embolism may follow severe contusions and acute osteomyelitis. Though comparatively infrequent, it is interesting to note that the forcible straightening—brisement forcé—of a contracted limb and ankylosed joints may terminate fatally as a result of this complication. At least three cases have been reported by Wahncan,[11] Colley,[12] and Ahrens.[13] In the last case the patient died in coma on the third day, and upon examination of the tissues it was found that the bones entering into the formation of the joint had been injured, and upon microscopic examination of the lungs an extensive fat embolism was discovered.

Pathology.—The fat corpuscles first lodge in the capillaries of the lungs, and if present in small quantities they may be forced on into the general circulation and be disseminated without giving rise to any serious disturbances. When present in larger quantities they may cause sufficient disturbance of the pulmonary circulation to give rise to a serious and perhaps fatal lesion. An examination of the lung tissue in this case will find numerous fat emboli, pulmonary infarcts, hyperemia, and edema; the alveoli are filled with red corpuscles, with fibrin, and with large and small white corpuscles. If the patient survives the effects of the pulmonary complication and the heart action is sustained, the fat corpuscles will be forced into the general circulation and lodge in the various organs, particularly the liver, kidney, brain, and cord, less frequently in other organs and tissues. In cases of fat embolism experimentally produced Schriba found the following lesions: In the kidney the glomeruli were plugged with numerous clusters of fat cells, and here and there, especially beneath the capsule, were seen small ecchymotic areas. The liver was the seat of a marked venous congestion, and frequently fat cells were seen on the periphery of and within the acini. The most important findings were in the brain and cord. The veins of the pia were filled with dark blood and the arteries were completely or almost empty. On cross-section numerous hemorrhagic foci were evident, and red blood-cells in considerable quantity were observed in the perivascular spaces. In some cases the tissue was edematous, in some a sero-sanguineous fluid was found in the ventricles, and in some there were areas of softening and capillary apoplexies. The emboli were most abundant in the vessels of the pia and the choroid plexus. In several cases emboli were found in the stomach, intestine, bladder, heart, muscles, skin, and in the vessels of the choroid and retina. In five fatal cases of fat embolism of the brain reported by Hämig [14] the lesions found at autopsy consisted essentially in a number of small ecchymotic areas in the gray and white matter, in the pons, medulla, and central ganglia; in one case the dura and pia were congested and edematous. The oil is finally disposed of partly, according to Beneke,[15] by a process of oxidation and saponification effected by a ferment in the blood-plasma, partly through the metabolic and phagocytic activities of the leukocytes, and partly by the liver and kidney.

Von Bergmann in 1873 was the first to recognize during life a case of fat embolism, which was subsequently confirmed by autopsy. Prior to that time there was a great diversity of opinion as to the importance to be attached to this phenomenon. Wagner[16] held them responsible for the development of metastatic abscesses, and others in that period held similar views. Later Busch[17] maintained that pure fat could not be held responsible for an inflammatory lesion and regarded fat emboli as of no consequence unless present in tremendous quantities. Earlier observers were also at great variance as to the cause of death. Schriba was quite positive that death could not be due to disturbance of the cardiac function, but was willing to admit that fat embolism could prove fatal only when it involved extensively the central nervous system. He even went so far as to say that there could not exist so high a grade of fat embolism of the pulmonary capillaries as to cause the death of the patient. These views are now only of historical interest. It is an accepted fact that the patient may die solely from the effects either of the pulmonary complications, or of lesions of the central nervous system. The termination of the case may be influenced by the disturbance of the renal function, as in a case reported by Colley,[12] in which the patient's death was attributed to fatty degeneration of the heart muscle.

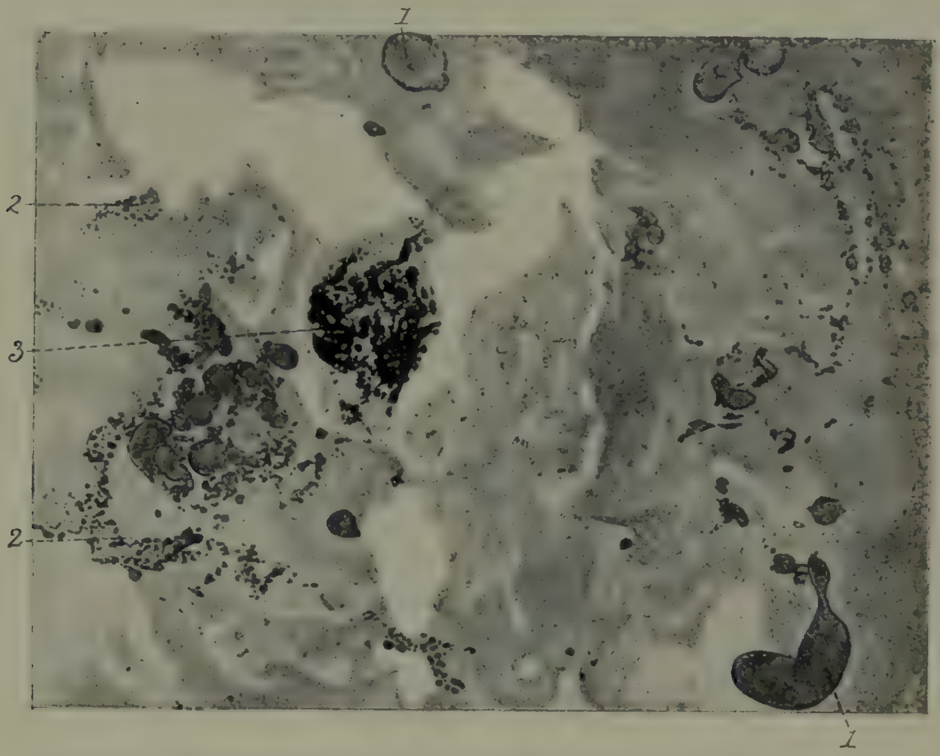

Fig. 129.—Fat-embolism in Fracture of the Thigh. × 78.
1, Large sausage-shaped masses of fat in the pulmonary arteries; 2, fat in the capillaries of the alveoli; 3, coal-pigment (Dürck).

Symptomatology.—By far the greatest portion of the contributions upon this subject is devoted to experimental studies and to the pathology; scant mention is made of the clinical picture. The symptoms upon which the diagnosis is based vary according to the organ or number of organs involved. Payr [18] suggested that we recognize two varieties of fat embolism, one the respiratory, the other the cerebral, according to whether the pulmonary symptoms or the cerebral symptoms are the predominating features in a given case. Inasmuch as the fat emboli first lodge in the lungs, the earliest symptoms, as a rule, are those which result from the pulmonary embarrassment: rapid respiration, dyspnea, and pallor followed by cyanosis and failure of the circulation, the expectoration of frothy, blood-stained mucus, together with the physical signs of pulmonary edema. If the symptoms develop within a few hours of the accident they may be masked somewhat if the patient is also the subject of shock. As the lungs become more and more edematous the action of the heart becomes correspondingly embarrassed. The subsequent phenomena depend, of course, upon what other organs are involved. Next in frequency to the thoracic complications are those of the brain. The cerebral symptoms are indicative of a diffuse rather than a local process, and consist usually of delirium, somnolence, and coma, and are due to embolism, hemorrhages, and thrombosis. In but two cases, according to Hämig,[15] was there localized paralysis; in a few vomiting, trismus, and general convulsions were noted. The temperature is usually normal or subnormal unless affected by some complication, and the urine contains fat and albumin. In exceptional cases ecchymosis may be seen upon the skin, mucous membrane, or in the conjunctiva. An ophthalmoscopic examination should always be made, as the diagnosis, as in one case, may be established by the appearance of the eyeground. In this case there were hemorrhages, fat drops in the vessels, and choked disc. The interval of time elapsing between the time of the accident and the appearance of the first symptom varies from a few hours to a number of days. It is as difficult to explain this great variation in the time at which the symptoms first make their appearance as it is to explain why in some cases a small amount of fat, in others a large amount, is required to give rise to any disturbance, and why the great majority of those having sustained similar injuries suffer no ill effects.

Diagnosis.—Shock is the condition with which, at least in the early stages, fat embolism is most likely to be confused. In differentiating between these two conditions it should be remembered that the symptoms of shock follow almost immediately after the accident, whereas in most cases the symptoms of fat embolism do not appear for a number of hours. The situation and character of the injury must always be taken into consideration. In shock the temperature is subnormal, the respirations shallow, the patient is pallid; in fat embolism the patient is cyanosed, the temperature normal or slightly subnormal, and the respirations stertorous. Acute pulmonary affections of other origin must be discriminated from those of fat embolism, and acute suppression of urine after serious accidents or operations should arouse one's suspicions as to the presence of fat embolism. It should be borne in mind that in cases in which the fat comes from an infected source acute or chronic septicemia is a possible complication or sequel. It may be a difficult matter to distinguish between the cerebral symptoms of fat embolism and those due to ordinary embolism, apoplexy, or traumatic hemorrhage. In both cases there may be coma, unconsciousness, localized paralyses, convulsions, preceded by an interval of consciousness, but in fat embolism there will usually be pulmonary complications; the pulse is rapid and weak, not the full and slow pulse of increased intracranial tension; focal symptoms (hemiplegia, monoplegia, and convulsions) are unusual, there may be ecchymotic areas in the skin and mucous membranes, and an examination of the eyeground may detect fat drops in the retinal vessels and choked disc. In every case of suspected fat embolism the urine should be examined. While in exceptional cases oil drops may not be detected in the urine, their presence would confirm the diagnosis. Specimens of urine or tissues suspected of containing fat globules should be fixed with osmic acid, which stains the fat black.

Treatment.—As there is no specific remedy the condition must be treated symptomatically. Inasmuch as additional quantities of fat may continue to enter the circulation, absolute rest of the affected part must be insisted upon. Remedies should be administered, as in air embolism, to sustain the heart in its efforts to force the globules through the pulmonary capillaries and to relieve the embarrassed respiration; strychnin, ammonia, and digitalis may be given for their stimulating effect. Nitrite of amyl has been recommended because it will produce a dilatation of the peripheral vessels as well as those of the lung. The propriety of giving a remedy which will diminish the peripheral resistance in the vessels and thereby throw upon the heart the additional strain necessary to maintain the normal blood-pressure may be questioned. Inhalations of oxygen should be tried, not only to sustain life but to favor elimination of fat by the process of oxidation.

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CHAPTER XI.

ERYSIPELAS.

By Charles Harrison Frazier, M.D.,

PHILADELPHIA.

Definition.—Erysipelas is an acute infective inflammation of the skin or mucous membranes, of febrile nature and varying severity, caused by the entrance through a wound or abrasion of a streptococcus and tending to spread through the lymphatic system.

Historical.—There is reason to believe that erysipelas was known to the ancients, and Hirsch[1] states that it has occurred in sporadic form at all times, and, with the exception of the tropics, in all regions of the earth's surface alike. It is usually stated that authentic records do not date farther back than the latter part of the eighteenth century, but several dissertations were written in the sixteenth century (Ellinger, 1560; Heurnius, 1596) and a number during the seventeenth century, among them one by Sydenham in 1685. Severe epidemics occurred in France in 1750, and Zuelzer[2] states that in Paris there died, on the average, in the years 1865 to 1869, about 350 persons annually. He also quotes Farr, that in England from 1862 to 1867 erysipelas was recorded as the cause of death in 3904 children under five years of age and in 4731 older persons. It is interesting to note that Anders,[3] writing in 1893, shows that in 781 cases of erysipelas only 10 were under ten years of age. Hirsch and various American authorities describe an extensive and virulent epidemic which prevailed in North America during 1841 to 1854, and Savary[4] reported an extensive outbreak of erysipelas at St. Bartholomew's Hospital, London, in 1873. Since then there have been no reported epidemics of any severity.

The accounts of these epidemics show that the disease was much more virulent than is even seen at the present time. In the surgical wards of the hospitals when the disease would be raging, every incision, every blister, even leech bites, seemed points of inoculation for the starting of erysipelas. The type of disease was variously termed *typhoid, malignant*, or *gangrenous*, and in the epidemic in this country Warren[5] quotes that "the discharges were said to be so acrid as to affect the instruments used in opening the abscesses, rendering them entirely unfit for further use."

Erysipelas in the older text-books has often been divided into the medical, idiopathic or facial variety and the surgical or traumatic form. Since the etiology of the condition has been definitely known to be microbic, such distinctions are of no value, as a wound, however minute, is always the portal of entry for the infecting organism. The contagiousness of erysipelas has been recognized for a long time and was proved even before the streptococcus was discovered. The nature of the cause was variously attributed to bilious states, the blocking up of the pores of the skin preventing the escape of acrid material from the blood, and in the early part of the nineteenth century was classed as an acute exanthem, along with scarlatina, variola, etc. Volkmann[6] in 1868 laid particular stress upon the traumatic origin of all cases of erysipelas. In the same year Hueter[7] maintained the identity of erysipelas and hospital gangrene, and Recklinghausen, Billroth, Ehrlich, Tillman, and Koch[8] found microörganisms in the lymphatic channels in the inflamed skin. In 1883 Fehleisen[9] cultivated the Streptococcus erysipelatis and for some years it was considered as the specific cause of erysipelas. Since Petruschky[10] in 1896 showed that the Streptococcus pyogenes may cause erysipelas in man, it is argued by nearly all authorities that the two organisms are identical. More recently Jordan[11] reaches the conclusion that erysipelas is not a specific disease, and while usually produced by the streptococcus, can be caused by the Staphylococcus aureus. He even regards as unsettled the question whether the facultative pus-producing organisms, such as the colon bacillus, the pneumococcus, or the typhoid bacillus, may not also produce erysipelas.

Etiology.—Erysipelas is comparatively rare before the age of puberty and also in old age. Anders[12] in a collection of 781 cases found the average age to be twenty-nine years, 36 per cent. occurring between the ages of twenty and thirty, 20 per cent. between thirty and forty, 17 per cent. between forty and fifty, and 14 per cent. between ten and twenty. Under ten years of age and over seventy years about 0.1 per cent. occurred in each decade. Males are affected more frequently than females—three to two, according to Anders; and the same writer states that the winter and spring months, more particularly the latter, influence the susceptibility to this disease. He found that one-half of 2010 cases occurred during the months of February, March, April, and May, and about 16 per cent. during the month of April alone.[13] Erysipelas, as has been stated, is due to a streptococcus obtaining a point of entrance in a traumatic or operative wound or a minute abrasion or fissure so small as to escape detection. It has been suggested that the organism may gain an entrance through the lungs or digestive tract, and particular attention has been directed recently to the naso-pharynx as a portal of entry, especially in the form known as facial erysipelas. Anders in 1893, in his study of the etiology of erysipelas, states that of 301 cases, acute coryza preceded the attack in 13 instances, and he suggests that slight lesions of the Schneiderian mucous membrane may favor specific infection. Much more recently Farlow[14] states his belief that the nasal septa, from their liability to erosion or ulceration, may be the entrance point for organisms which later cause facial erysipelas. The pharynx, tonsils, middle ear, scalp, or the finger-nails when used in scratching may all be points from which the streptococcus may be disseminated. Associated as predisposing causes may be mentioned such chronic diseases and conditions as chronic nephritis, phthisis, etc., poverty, inanition, exhaustion, overwork, previous illness, etc., which act by lessening the resistance of the tissues.

The most common seat of erysipelas is upon the face and scalp, probably 90 per cent. occurring in these localities; and of the remainder, the leg and foot supply nearly all the cases.

The contagiousness of erysipelas has been previously referred to, and the modern idea has recently been emphasized by Franke,[15] who states that the erysipelas patient is no more dangerous as a source of contagion to his fellow-patients than one with a suppurating wound of the hand, so long as he does not scratch the patches. The disappearance of the extreme isolation idea for these cases has only kept step with our improved methods in asepsis and antisepsis and with the lessening of pyogenic infection as a complication in any wound, whether traumatic or operative.

Some curious susceptibilities to erysipelas have, however, been reported from time to time, when, in spite of all possible precautions against infection, an attack has occurred after each fresh exposure. This observation is akin to those where an individual, even of cleanly habits, suffers during a lifetime from frequently recurring furuncles.

The relation of erysipelas to *puerperal fever* has long been recognized, and Oliver Wendell Holmes was particularly preëminent among those who recognized this fact. "While not the first to preach this doctrine, yet to him belongs the credit of having forced men to listen to the truth."[16]

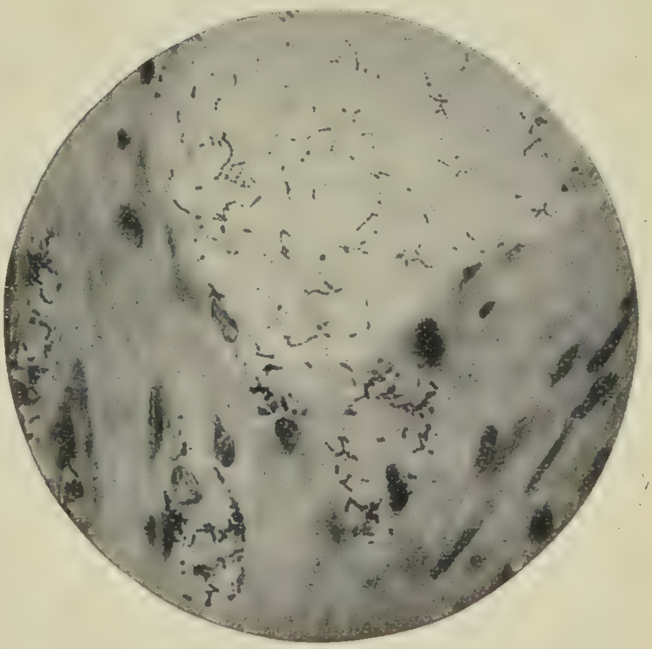

FIG. 130.—STREPTOCOCCUS ERYSIPELATIS, SEEN IN SECTION OF HUMAN SKIN. × 500 (Fränkel and Pfeiffer).

The period of incubation of erysipelas has been estimated to be from fifteen to sixty hours.

Pathology.—Erysipelas is a progressive lymphangitis, the surrounding tissues being secondarily implicated by contiguity. The streptococci enter the lymph-vessels through the wound in the skin, multiply therein, and, using the lymph spaces and vessels as pathways, rapidly spread into new areas marked by an advancing wave of redness and swelling. This spread must be one of continuous growth of colonies, because the streptococcus is non-motile and in sections of the tissues the organisms are found to densely crowd the lymph spaces or vessels. They are most abundantly demonstrated at the margin of the spreading redness and are much less abundant in the first areas affected. The microorganismal invasion is accompanied by a cellular and serous infiltration, the smaller blood-vessels becoming filled with leukocytes which escape in large numbers into the surrounding corium and surround the vessels, the hair-follicles, and the sudoriparous glands. The exudate often becomes serofibrinous and gives the tense, firm, edematous feel to the inflamed tissues. The infection may spread beneath the horny layer of the skin and cause its desquamation, or in severe cases the entire epidermic layer becomes liquefied and converted into purulent vesicles. In these severe cases the corium may also become the seat of necrosis and *gangrenous erysipelas* will occur. If the infection spreads to the deeper subcutaneous tissue, extensive infiltrations may be followed by necrosis, when *phlegmonous erysipelas* and *cellulitis* will be noted. The difference pathologically between these clinical forms is practically one of degree only.

Metastatic infection may occur and the organisms be carried by the blood-stream to lung, liver, heart-valves, kidneys, bone-marrow, joints, etc. The local inflammation, the high fever, great prostration, etc., are due to the absorption of the highly poisonous toxalbumins generated by the streptococcus. It is interesting to record that while a streptococcus infection is ordinarily a very acute condition, yet sometimes a deep and widespread cellulitis occurs with a "wooden" hardness to the tissues and without fever. Krause,[17] Kusnetzoff,[18] and others have described such cases as being due to the formation of granulation tissue and the proliferation of the fixed connective-tissue cells without circumscribed areas of suppuration. This cellular proliferation may also occur in the acute form, and in all cases cellular activity is present some time after the disappearance of the streptococci from the tissues. In fatal cases intestinal ulceration, congestion of the brain and meninges, and parenchymatous degeneration of the spleen and kidneys may be observed.

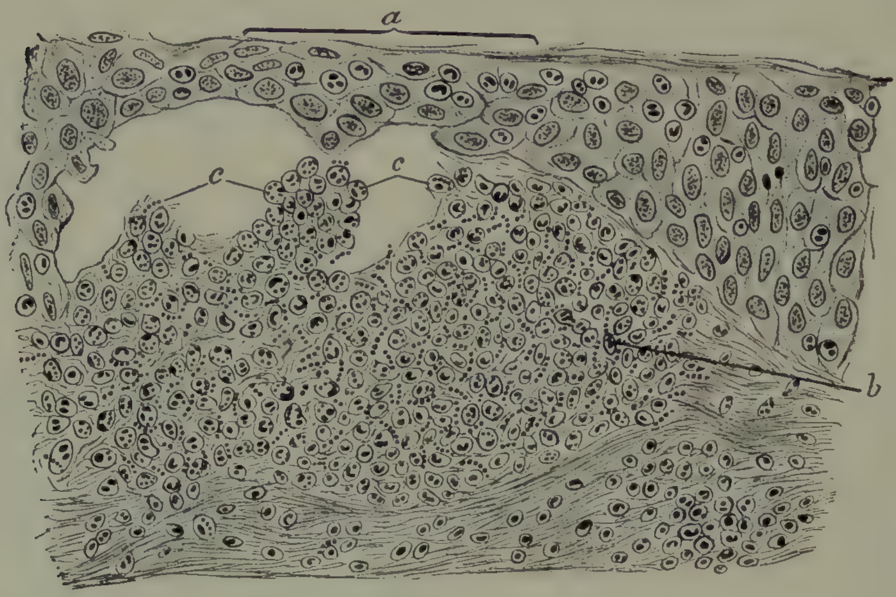

FIG. 131.—ERYSIPELAS OF THE EYELID.
a, Epithelial layer invaded by occasional leukocytes; *b*, invasion of subepithelial tissue by streptococci and leukocytes; *c*, *c*, streptococci inclosed in leukocytes (Weichselbaum).

Symptomatology.—The first warning that erysipelas has occurred from a wound is given almost without exception by a chill, which may amount to a rigor, especially in childhood, and is accompanied by vomiting and more or less gastric disturbance. These first symptoms are often disregarded because an examination of the wound shows no perceptible change. The temperature rises rather rapidly, and in twelve to fourteen hours reaches 102° to 105° F., at which point it becomes continuous with but little diurnal variation. The tongue becomes coated, and headache, thirst, anorexia, and a feeling of distress in the epigastrium are experienced. The pulse is full and bounding and toward evening the patient becomes delirious. The nearest lymph nodes become enlarged and tender and the urine is of high color and charged with urates. In twenty-four hours the patient complains of a feeling of burning and distention or tightness in the wound, and a careful examination at this time discloses the fact that skin around the seat of infection is dusky red, swollen, with a zigzag or wavy border which has been likened to the burnt edges of a sheet of paper. Palpation shows the firmness of the skin from the serous exudation, and if the wound has been suppurative in character the purulent nature of the discharge changes to a serous one. After withdrawing the pressure of the examining fingers the skin often presents a yellowish hue. In the severe type the skin becomes raised, forming vesicles and bullæ filled with a clear, straw-colored fluid, becoming turbid and purulent, the discharge of the fluid being followed by scaly yellow or brownish scabs. The inflammatory swelling slowly advances with the serrated or zigzag border before mentioned, almost always with a sharp border at the point of junction with the healthy skin, this being one of the cardinal symptoms of the disease. The spread of erysipelas does not occur along any regular lines and may extend for some distance from the point of infection, having the curious distinction of abating in the older areas of infection while rapidly creeping into new ones. After some days the fever curve becomes irregular, abating as the process subsides and ascending as new areas light up, often in the parts originally involved, not reaching the normal until the dermatitis has subsided. During the latter part of the attack there is marked prostration and the pulse becomes rapid and weak.

The duration of erysipelas is very variable, and it may run a typical course, ending in recovery within two days, or may be protracted over weeks. Anders found that the average duration in patients under forty years of age was about fourteen days, while in persons of a later period of life, especially if enfeebled by some chronic disease, it was much longer. Relapses are frequent and occur in about 10 per cent. of cases, especially if the general health is impaired at the time of the attack. Warren believes that many recurrences are due to an auto-inoculation from the clothing of the patient, and he disinfects the patient, changes his clothing, and removes him to a different room upon the subsidence of the febrile disturbance. Toward the close of the disease exfoliation of skin occurs, and sometimes a subnormal temperature may persist for some days, with great weakness, although, as a rule, the patient recovers completely, showing no ill effects from the attack. Recurrences may also occur some months after the original attacks, and these are often fatal in patients enfeebled by the long continuance of a suppurating wound.

Varieties.—**Phlegmonous erysipelas** is that form in which the infection extends downward into the subcutaneous tissues and, being of a more virulent nature, induces more serious symptoms. Suppuration is rarely seen in cutaneous erysipelas and is probably caused by a virulent variety of streptococcus. When the deeper tissues are invaded the picture of erysipelas is overshadowed by the more distinct local lesions of the phlegmonous inflammation, the fever continues high, often typhoidal in character, fluctuation or bogginess is felt, and the skin rapidly becomes undermined by the foul, acrid pus. Free incisions liberate great quantities of pus, in which may be found shreds of the necrotic connective tissue. The suppuration may extend for a considerable distance under the skin, causing its gangrene, between muscle planes, effecting their necrosis; and in severe but fortunately rare cases the periosteum, the bones, or the joints may be involved in the process of disorganization. If phlegmonous cellulitis attacks the face, severe disfiguration and even blindness may result, or the infection extend into the cranial cavity and cause a fatal meningitis.

Facial erysipelas may occur after operations upon the face, such as rhinoplasty, after fractures of the nose, or in the so-called "idiopathic" variety without ascertainable cause, although, as has been mentioned, these undoubtedly result from wounds of the epithelial covering of the nose, pharynx, or ear. After the premonitory symptoms have been developed there is noticed a redness at the nasal orifice, at the angle of the eye, about the ear, or other parts of the face or head. In a few hours this area has greatly enlarged, and, spreading like a drop of oil on paper, invades the greater part of the face, the chin alone usually escaping. The inflammatory area on the nose and cheeks often is of a butterfly shape during the first twenty-four hours, but later spreads over the forehead and scalp to the nape of the neck. The face becomes of a scarlet red color, the swelling and edema are excessive, the face feels hot and burning, and the patient often complains of itching. The disease has the characteristic sharply defined border, the tendency to spread irregularly with recovery in the portions first involved, the vesicles or bullæ, and the constitutional reaction before described. In many cases the swelling is so marked as to obliterate the facial expression and close the eyes. The pain may be intense, particularly when the scalp is involved, and in the latter event severe headache and delirium are almost constant symptoms, associated with very high temperature. Early in the attack the submaxillary lymph nodes become enlarged and tender. After recovery from erysipelas of the scalp the hair falls out from the loosening of the hair shafts through the serous exudation into the hair-follicles, but will return again.

Erysipelas is occasionally found in the mucous membranes, the nasal cavity, pharynx, larynx, Eustachian tube, middle ear, vagina, or rectum. A very few cases have been reported where the disease has extended through the gastro-intestinal tract, and Schönlein [19] states that in times of extensive epidemics many otherwise healthy persons living within the affected district were attacked by severe diarrhea, without the occurrence of any erysipelatous process upon the skin. The most common of these rare forms is that of the pharynx, which becomes intensely congested, painful, burning, and dry. There is difficulty in swallowing and a membranous exudate, abscess, or edema of the glottis may occur, and pneumonia has been observed from the extension of the process downward.

Erysipelas neonatorum is acquired by infection at the umbilicus and is usually observed in epidemic form in hospitals. The abdomen is first involved, later the genitals and thighs; the umbilical veins frequently become filled with a septic thrombus extending toward the liver. Local symptoms are very intense, internal metastatic collections occur, and death usually follows by the sixth or eighth day.

Diagnosis.—Erysipelas may be confused with simple lymphangitis, erythema, inflammation about stitch abscesses, phlegmonous cellulitis, malignant edema, or possibly the edematous form of anthrax.

In *simple lymphangitis* the redness and swelling extend along the course of the vessels, but there is no typical dermatitis with irregular peripheral extension and central recrudescence.

Erythema is a transitory hyperemia of the skin, seldom confined to a single point, without glandular induration, and is not followed by desquamation.

Stitch abscesses are often surrounded by an inflammatory area, but fever only of the constitutional disturbances will be present, and the removal of the suture and the application of a hot antiseptic dressing prevent the further spread within a few hours.

Phlegmonous cellulitis does not exhibit the well-defined border of erysipelas, is darker in color, of board-like hardness, and deeply seated. The difference, however, is but little, and often is not made by surgeons. Compound fractures, when infected, exhibit this type of purulent inflammation.

In *malignant edema* there is the rapid appearance of hemorrhagic edema, the dusky appearance of the skin, and the gas-bubbles in the foul hemorrhagic secretion.

Edematous anthrax lacks the high fever, the abrupt line of demarcation, and the early great prostration.

Prognosis.—Simple uncomplicated cases are rarely fatal unless infants or persons debilitated by age or chronic disease are attacked. Recovery is the rule, and should be borne in mind in estimating the value of any extolled remedy, of which there are legion. Anders estimates the mortality to vary from 3 per cent. during the third decade to 45 per cent. in patients over seventy years of age, with an average mortality of 6.5 per cent. Those cases following traumatic wounds gave a percentage of deaths of 14.5. Zuelzer, writing in 1875, states that in nearly 10,000 cases recorded by various authors the mortailty averaged 11 per cent. In the American Civil War the mortality (in surgical cases) was 11 per cent. The complications responsible for the mortality most often follow the phlegmonous forms, in which extensive necrosis results in septicemia, pyemia, hemorrhage, pneumonia, or nephritis. If the disease begins in the throat, edema of the glottis may occur; if in the vagina, pyemia or septicemia; if on the face, orbital suppuration may extend backward to the brain; or if on the scalp, the infection may extend to the brain by an extension of a thrombosis of the cutaneous veins through the emissaries to the longitudinal sinus. It has been especially noted that the mortality is high in alcoholic subjects who develop delirium tremens during the attacks and in those patients in whom delirium is active and prolonged.

As sequels to erysipelas, abscesses, rheumatism, pericarditis, endocarditis, pleurisy, nephritis, phlebitis, neuritis, etc., have been recorded.

Treatment.—It is usual to advise the isolation of the affected patient from all other persons, but such a procedure is often difficult of attainment and unnecessary as a rule. If the erysipelas is so located, as upon the face or perineum, where occlusive dressings cannot be applied, the patient had better be isolated until the symptoms of inflammation have subsided, when the isolation can be suspended, as there is no danger from the scaling. But in the ordinary case there is no more danger in an erysipelatous wound, *properly treated*, than in any other condition of wound infection, and the patient can be kept in the ward usually devoted to "pus" cases without fear of spreading the infection. As Franke has shown, the cocci induce a lymphangitis or an abscess, and never come to the surface in the vesicles nor cast off epidermis, any more than in a phlegmonous inflammation of a tendon-sheath. If the wound is protected by proper occlusive dressings, and scratching by the patient thereby prevented, there is no danger of disseminating the infection. Rubber gloves should always be worn while dressing an erysipelatous wound, the removed dressings destroyed at once, and the instruments used disinfected.

The local treatment of erysipelas comprises an assortment of lotions, solutions, and ointments whose name is legion, because the tendency of the disease is to rapid spontaneous recovery, and almost any local application does good in a large percentage of cases.

The simplest treatment is probably the best; the rigid antiseptic treatment of existing wounds or other lesions, cold compresses to relax the skin, rest, elevation of the limb, and incisions only if pus forms. Where the disease is spreading good results are said to be obtained by spraying the affected surface with a weak solution of corrosive sublimate in ether, or painting the borders of the affected area with contractile collodion. Subcutaneous injections of carbolic acid have been highly praised as a specific, but the result is doubtful. The ointments most commonly used are carbolic acid and lanolin, 1:100, and ichthyol (25 per cent.) covered with a thin layer of gutta-percha tissue or oiled paper. In facial erysipelas ice-cold compresses of Burow's solution (liquor aluminii acetatis) are about as efficient as anything else, and much less disagreeable to the patient and his friends than the usual ichthyol ointment (10 to 25 per cent.) used. The skin should first be cleansed of dirt, epithelial débris, and fatty matter, and then the solution applied. Solutions of bichlorid of mercury (1:4000 to 1:2000) or of carbolic acid (1 to 2 per cent.) may be used if the aluminum acetate is not obtainable, and should be applied cold and frequently renewed or covered with a thin, light ice-bag, containing finely cracked ice and sawdust. A number of writers, particularly Jarcho,[20] Ayer,[21] Smith,[22] and Davis,[23] still advocate the use of antistreptococcic serum. Newcomb,[24] Denyo,[25] Rosenthal,[26] etc., find it absolutely without effect in the disease. Ayer reports that the serum shortens the course of an uncomplicated attack of erysipelas considerably and also tends to inhibit the extension of the disease. He recommends an initial dose of 20 c.c., followed by doses of 10 c.c. as often as necessary. Fornaca [29] has treated nine severe cases of facial erysipelas with the serum of convalescents from erysipelas, with gratifying results in ameliorating the constitutional symptoms, although the local condition was not modified. Colloidal silver, potassium permanganate, iodin, the red-light treatment, etc., have also been advocated by recent writers. In the phlegmonous form of erysipelas it is important to recognize the suppuration as early as possible, when free incisions, removal of sloughs, and disinfection of the pus-cavities must be thoroughly performed. On the face incision is usually required along the infraorbital margin if pus forms, and in the perineum the median raphé is the best location for the incision.

Constitutional treatment should be directed to the support and stimulation of the patient. The bowels should be opened by small doses of calomel, followed by a saline, or by an enema in debilitated patients. The food should be light, nourishing, and carefully selected, hyperpyrexia treated by hydrotherapy; small doses of quinin and salol are beneficial, and strychnin or alcohol when required as a stimulant for the cardiac depression. Morphin must often be given (especially in facial erysipelas) to relieve pain and procure sleep. During convalescence exposure to cold or fatigue must be avoided, tonic medication given, and when the skin has returned to its normal condition a full bath given in alkaline water, and a complete change of bed, bedding, and clothing made. Local stimulations of the skin by alternate hot and cold ablutions and massage are beneficial to the skin. It is hardly necessary to add that all abrasions or wounds on other portions of the body should be carefully protected during the attack, because, after all, the best treatment of erysipelas is to prevent patients from having it.

The curative influence of erysipelas upon various affections has been noted for many years, the effect upon old eczemas, lupus, chronic leg-ulcers, old sinuses due to caries of bone, non-malignant tumors, recent wounds, etc., being the first to be commented upon. It was explained on the supposition that old infiltrations may be more easily brought to softening and resorption by the uniform intense inflammation of the skin and the altered relations of tension and hyperemia in the affected parts (Zuelzer). Fehleisen, and, among others, Spronk and Coley, have successively advocated the use of cultures of the streptococcus of erysipelas upon malignant growths, particularly on sarcoma. Coley has been advocating the treatment of inoperable sarcoma by the mixed toxins of erysipelas and of the Bacillus prodigiosus for some years, his first work dating back to 1891. In a recent paper [27] he also advises the use of the injections in all cases after primary operation as a prophylaxis against recurrence. In all inoperable cases he believes a trial should be made with the mixed toxins before amputating the limb, basing his assertions upon twelve cases, in eight of which the tumor disappeared and the patients were well from three to six years afterward. Other surgeons have not had such fortunate results, however, and the method is still on trial.

ERYSIPELOID.

A form of infective dermatitis first described by Rosenbach is produced by inoculation into the skin of the finger or hand of dead or decomposing animal matter, fish, or foul cheese. It is most frequently met with in cooks, butchers, fish dealers, etc. Rosenbach attributes the disease to an organism of the cladothrix variety. Gilchrist [28] has observed a large number of cases originating from crab bites. From the records of 323 cases he finds that the disease usually makes its appearance during the months of June, July, and August, when hard crabs are in season. A few days after a bite or an injury from a crab the fingers or hand affected present a painful, red swelling about the site of the injury, accompanied by local temperature and a throbbing sensation. The lower border of the elevated eruption is marked by a sharp red line of demarcation, tending to spread down the finger toward the hand, and thence to other fingers, the back, the palm, or both sides of the hand. The disease rarely attacks the forearm, still more rarely the feet, and does not suppurate or produce papules, vesicles, or pustules unless secondary infection occurs. Lymphangitis and lymphadenitis may occur, but are rare sequels. The temperature, pulse, and tongue are not disturbed.

Histologically erysipeloid is characterized by an invasion of polynuclear leukocytes throughout the corium, and a massing of lymphoid cells about the blood-vessels. Gilchrist failed to obtain results by culture, and suggests that it may be due to a special ferment, inoculated by the crabs in the skin. The treatment advised consists in the local application of a plaster of salicylic acid (25 per cent.) for three days, followed by some simple ointment. Injections of a 5 per cent. solution of carbolic acid into the advancing edge of the dermatitis and the use of iodoform ointment upon the affected parts may also be tried.

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CHAPTER XII.

TETANUS.

By Charles Harrison Frazier, M.D.,

PHILADELPHIA.

Tetanus is an infectious disease characterized by both tonic and clonic contractions of all the voluntary muscles of the body, beginning in the jaw and spreading to the trunk and extremities.

History.—Tetanus has been a well-recognized disease for centuries; even in Hippocrates one may find a very accurate description of the clinical syndrome, and it was known even then that the toxins had a special affinity for the nervous system. It was not until 1880, however, that any light was thrown upon its etiology as a specific disease. Sternberg[1] in 1880 announced that he was able to produce experimental tetanus in animals by injecting into them gutter water and earth. Four years later Carle and Rattone[2] produced tetanus experimentally by injecting into animals the pus from human tetanus. To Nicolaier[3] we are indebted for some of the most important observations upon the tetanus bacillus. He was the first to call attention to the presence of a long, delicate bacillus in the pus taken from tetanus wounds, which he had produced experimentally by introducing earth into small pockets at the root of the tail of mice, rabbits, and guinea-pigs. He observed, furthermore, that this organism was only found in the immediate neighborhood of the wound, and that when the earth was subjected to a temperature of 190° C. for one hour, the power of the organism to produce tetanus was destroyed. His observations as to the habitat of the organism were also interesting; except in wounds, the only place where he could find the organism was in the earth, and, what is of equal importance, only in the earths from certain sources, and only in the upper layers of the soil. He was able to grow the bacillus in culture media, but unfortunately, though he was convinced of its specificity, he was never able to obtain a pure culture. It was Kitasato's[4] good fortune to be the first to isolate a pure culture of the bacillus, the discovery of which must, however, always be accredited to Nicolaier. Kitasato's success in isolating the organism was due to his recognition of two important properties: first, that the spores were resistant to heat, and, secondly, that the bacillus was anaërobic and could not grow in the presence of oxygen.

With relation to the specific action of the tetanus bacillus upon the nervous system Gumprecht[5] was the first to show with some degree of certainty that the toxins attacked the spinal cord and not the peripheral nerves, and that all the clinical phenomena were the result of the action of the toxins upon the cord alone. In 1892 the presence of the toxins in the central and peripheral nervous system was demonstrated by Bruschettini. Up to this time the specific organism had been discovered, the organism had been isolated in pure culture, it was known that the disease was produced by action of the toxins generated in the wound upon the spinal cord, and the toxins had been found in the spinal cord and peripheral nerves, but the path along which the toxins traveled to the cord was still a matter of obscurity.

In 1894 Brunner[6] suggested in a case of head tetanus that the virus traveled along the facial nerve, and both Marie (1897) and Gumprecht were of the same opinion; but up to the year 1901 it was the prevailing opinion that the toxins reached their destination through the blood and lymph circulation. For our more exact knowledge of the action of the tetanus toxin and its means of transportation we must turn to the work of Marie and Morax,[7] and that of Meyer and Ransom.[8] Together these constitute the most noteworthy contributions of recent years.

The tetanus bacillus is long, slender and motile, appears in pairs or threads, and the development of a spore at one end gives to it its club-shaped or drumstick appearance. It grows in ordinary culture media, most rapidly at a temperature of 36° and 38° C. It is entirely anaërobic and flourishes in an atmosphere of hydrogen. The spores, unlike the bacillus, are very resistant to heat, to drying, and to the various germicides. The spores resist a temperature of 80° C. for an hour, and a 5 per cent. carbolic acid solution for ten hours. Exposure to a temperature of 100° C. for five minutes will kill in five minutes. A 1:1000 mercuric chlorid solution, according to Lambert,[9] will kill spores in ten minutes, a 1 per cent. nitrate of silver solution in one minute, and a 1:1000 in five minutes, a 5.5 per cent. solution of carbolic acid and a 0.5 per cent. of hydrochloric acid will kill in ten minutes. The bacillus liquefies gelatin and the bacilli accumulate at the bottom of the tube. Before this happens the bacillus sends out irregularly shaped ray-like processes, which have been compared in appearance to a fir tree. Its normal habitat is the soil, especially the soil about stables or in gardens richly manured.

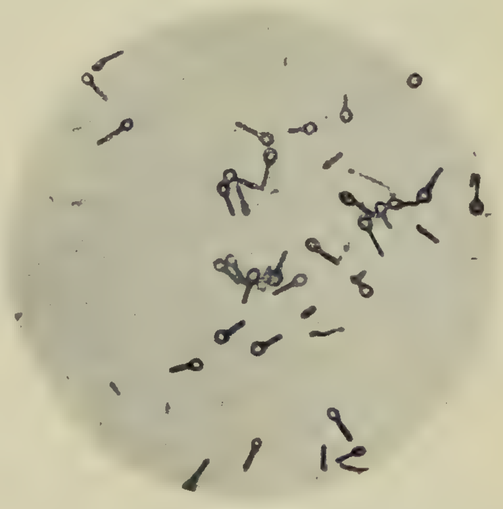

FIG. 132.—BACILLUS OF TETANUS WITH SPORES (Fränkel and Pfeiffer).

Pathogenesis.—A discussion of the causation of tetanus bacillus to be comprehensive, must be a clinico-pathologic one, must make reference to the conditions under which tetanus is acquired and the conditions to which it gives rise once the organism is lodged in the tissues. In so far as the clinical aspects are concerned, it is well known that the tetanus bacillus is carried into the body in most instances by objects which have been soiled with earth and dust, or the discharge from wounds already infected. It has been suggested that tetanus may be acquired by the ingestion of new vegetables or the inhalation of air (Rogers [10]), and that this may account for some of the cases of obscure origin. The character of the object which inflicts the injury is usually one which produces a punctured wound; thus, in many instances tetanus follows the wound of the popular "rusty nail," splinter, or pitchfork. The anaërobic character of the bacillus permits it to flourish only in tissues which do not communicate with the external air. A very common cause, however, of tetanus is the injury inflicted by a gunshot or pistol-shot wound, or by the toy pistol so popular with the younger element in this country on the Fourth of July. Thus, of thirty-two wounds from the wads of toy pistols treated at the Hudson City Hospital (Taylor [11]) three were followed by fatal tetanus. During the fortnight preceding and following the Fourth of July about 2000 wounds were treated, and of these only two developed tetanus, one due to a powder burn and the other following a cellulitis after an amputation of the finger. In order to determine the cause for the relative frequency of tetanus after wounds with toy pistols Taylor made an investigation of the wads to ascertain whether they contained the tetanus bacillus. He purchased many boxes of cartridges from different localities during the summer of 1899; the wads were carefully removed, macerated in bouillon tubes, and subjected to a temperature of 75° to 80° C. for thirty minutes to eliminate the less resistant organisms. Cultures were made, but none were found to contain a bacillus with the characteristic morphology of the tetanus bacillus.

These observations have been repeated at various times with similar results. As many as 759 blank cartridges manufactured by different concerns, at different times and in different cities, have been examined, and with a single exception the reports were absolutely negative.[12] The list of predisposing factors would not be complete were reference not made to tetanus as a complication of vaccination. Both McFarland [13] and Willson [14] have published excellent papers upon this topic. That this is not a recognized complication of tetanus might be inferred from the "minority report" of the British Commission, published in 1896, in which but a single case is mentioned, although the disadvantages of vaccination were carefully and forcibly summarized. The scarcity of cases appearing in literature is due, McFarland suggests, to the desire to conceal the facts from the public. Of the ninety-five cases which he collected, but fifteen were found in literature. A chronologic study of the cases showed that from 1839 to 1902 sixty-three of the ninety-five cases occurred in 1901, and they all occurred in America, the complication being unknown in the European countries. It was further observed that a very considerable proportion of the cases developed after the use of the virus manufactured by one particular firm. McFarland concluded from his investigation that the tetanus organism may be present in the vaccine virus in small numbers, being derived from the manure and hay; that through carelessness in the management of the wound or by accident the number of bacilli became still greater, and that the future avoidance of the complication was to be sought for in the preparation of the virus. Willson was more inclined to attribute it to the vicious use of the vaccination shield and to the general disregard of the principles of asepsis or antisepsis in the treatment of the vaccination sore.

As a possible etiologic factor mention should be made of the use of gelatin as a hemostatic. Intravenous and subcutaneous injections of gelatin for the control of internal hemorrhage, as in typhoid fever, and for the treatment of aneurisms have been used since 1896. At first they were thought to be perfectly harmless, but recently these injections have been complicated in some cases by tetanus. Thus Kuhn [15] reported a case of tetanus following the injection of gelatin as a hemophiliac; Gerulanos, Georgi, and Lorenzo [16] reported four cases after operations, as for subphrenic abscess. Hochalt and Herezel [17] reported a case developing on the seventh day after an injection following a splenectomy. Levy and Bruns [18] found the tetanus bacillus present in commercial gelatin; they examined six samples of gelatin and found the bacillus in four. In reviewing their work Anderson [19] concluded that when gelatin is to be used for injection it should be boiled at least ten minutes, on account of the variability of the thermal death-point in different species. Whether this amount of heat impairs the hemostatic effect has not been settled. In hospitals it is perfectly possible to render the use of gelatin absolutely safe by sterilizing it by the fractional method on three successive days and storing it in sterile jars.

Considering now the etiology as it relates to the specific action of the tetanus bacillus, we will refer to the mode of entrance, to the immediate effect upon the tissues, to the generation of its active principle, to the spread of the toxins, and their effect upon the tissues of the spinal cord.

The tetanus bacillus probably gains access to the tissues through a wound or abrasion of the skin and mucous membranes, inflicted by an object which was contaminated with the discharge from previously infected wounds or with tetanized diet. In order that the bacilli may grow and flourish the wound must be of such a character as not to give ready access to the air, or, as McFarland [20] suggests, its entrance must be accompanied by some other microörganism whose marked affinity for oxygen shall absorb all the oxygen contained in the tissues so rapidly as to allow the tetanus bacillus to grow. Vaillard and Rouget [21] found also that there were other conditions affecting the growth and activity of the organism; when the tetanus spores were freed from their toxins they were innocuous when not accompanied by another bacterium. When the spores were introduced without their toxins they were destroyed by the phagocytes; but when they were introduced with their toxins the tissues were so damaged by certain chemical substances that they were not able to check the growth of the organism. The tetanus bacillus is not a pus-producing organism and therefore causes but little reaction in the wound. It is more than likely that the suppuration in the wound is the result of a mixed infection.

Inasmuch as the tetanus bacillus, like the diphtheria bacillus, is only found at the point of original inoculation the lesions and symptoms to which it gives rise must be the result of the toxic substances which it generates in the wound. While Brieger[22] in 1887 succeeded in isolating from an impure culture the two substances, tetanin and tetanotoxin, which, although fatal in small doses, did not produce the typical convulsions, it was not until later that the true nature of the toxin was discovered. The work of Fraenkel[23] (1890) and Kitasato[24] showed this to be a toxalbumin, capable of killing a mouse in infinitesimal doses (0.00001 c.c.). The toxin has been separated from two distinct bodies, tetanospasmin and tetanolysin, one causing the typical spasms and the other destruction of the red blood-corpuscles.

Having discovered the precise chemical nature of the toxic substance, it remained to determine its mode of dissemination and its physiologic action. First, as to its mode of dissemination. According to the most recent investigations, the changes in the peripheral nerves are not so constant as to afford an explanation for the clinical phenomena. The so-called "nervous theory" of tetanus was based upon the old macroscopic observations of Larrey, Friedrich, Remak,[25] and others, who marked inflammatory changes in the nerves between the site of infection and spinal cord.

The more recent observations, based upon microscopic examinations, prove that the lesions in the nerves, if present at all, are not marked and are found only in the neighborhood of the wound. Thus in one case there was a neuritis of the popliteal nerve, in another of the sciatic, and in another of the tibial; Achard[26] examined the nerves in four cases of tetanus and found in three some degeneration of a few fibers which he believes was secondary.

In contrast to these positive findings we have negative findings of Joffray, Poncet, Nechaud, Pitres, and Vaillard,[27] all of whom believed the tetanus toxin could reach the cord by the blood channel, independently of the lymphatics. It is more than likely, Liberti says, that the occasional changes in the nerves are rather the result of an ascending neuritis, which owes its origin to the inflammatory process in the wound. If the wound is not infected or if the disease runs a very rapid course, the nerve lesions may be insignificant or there may be none at all. The investigations which Liberti made to determine this question, at least in so far as concerned animals, were entirely negative. Brunner[28] stated, as a result of his studies, that the anatomic lesions of the central nervous system were uncertain and generally negative. He was not able to show any characteristic changes either in the spinal cord, brain, or peripheral nerves. In 1897 Marinesco[29] found decided changes, especially in the cells of the anterior horns. These consisted in intense staining of the axis-cylinders, variation in stain, and irregularities in the shape of the nuclei. These conditions, however, were found in animals which he had killed and not those which had died of tetanus spontaneously. According to Nissl, the nucleus of the nerve cells is smaller, more angular, and homogeneous. As a result of a series of experiments Goldscheider and Hatan[30] concluded that the changes found in the nervous system were quite characteristic of tetanus, and could not be mistaken for any other disease. The morphologic changes in the cells corresponded precisely with the clinical manifestations in animals which died from tetanus. DeBuck and Moor[31] and a number of others observed marked staining of the protoplasmic processes, and, within the cells, fissures and vacuoles. Other observers have noted this vacuole formation from animals which died of experimental tetanus. Liberti found in the motor cells first enlargement, and, later, a breaking up of the Nissl bodies, regeneration of the latter, and, sometimes, a swelling of all the cells, even the nucleoli. The Nissl bodies assumed a somewhat angular shape. The more rapid the disease, the more striking were these changes. In other cases the cells presented a homogeneous appearance and could no longer be recognized; in some there were numerous and large vacuoles, in others one met with large numbers of *glia-kerne*—sometimes in the nerve cells, and at other times within the cell bodies. Liberti does not believe, as Marinesco does, that the glia cells destroy the nerve cells, but that the latter crowd around the glia cells and force them to penetrate the nerve cells. As a result of his experimental observations he claims that the effect of the tetanus toxins upon the motor cells is perfectly evident and constant. The *alterations in the cell structures are not, however, pathognomonic of tetanus; they are seen in other infections, and cannot therefore be said to be of diagnostic value.*

The most important contribution to our knowledge of the development of the disease, second only in importance to the discovery of the bacillus, the toxins and antitoxins, is the work of Meyer and Ransom.[32] Up to within a year or two of the publication of the results of their experiments it was the prevailing opinion that the toxins were carried to the spinal cord by the blood and lymphatics. It remained for Meyer and Ransom to prove that the toxins were carried to the spinal cord not by the lymphatic circulation but by the nerves. After subcutaneous inoculation of the toxin into the hind-legs of rabbits, they were able to demonstrate it in the sciatic nerve. Furthermore, they proved that the toxins are carried only to the cord by the motor, never by the sensory nerves, and, finally, that the toxins are carried not by the lymph channels in the nerve, but in the protoplasm of the neurone. Complementary to the results of Meyer and Ransom were those of Marie and Morax.[33] The transmission of the toxins to the cord by the nerve depends upon the integrity of its axis-cylinders. Thus it was found that when degeneration was set up by section of the nerve prior to inoculation the nerve would not take up any toxin; and, furthermore, if the nerve was cut before the inoculation, the toxins were found in the distal but not in the proximal portion, thus proving that the toxins were not carried by the neural capillaries, but by the axis-cylinders. These results should not be interpreted as precluding the possibility of tetanus developing even when the nerves of the limb in which the toxins were injected have been divided. When the toxins are injected into the body, some of the toxin diffuses itself through the tissues until it comes in contact with the terminal filaments of a motor nerve, through the medium of which it is transmitted to the motor ganglia of the cord. The rest of the toxin is taken up by the lymphatics, enters the general circulation, where it is distributed by the capillaries, and is thus brought in contact with the motor nerve-endings throughout the body. When it reaches the cord it travels always upward until it reaches the vital centers of the medulla. The sensory nerves play no part in the transmission of the toxin, at least in the clinical manifestations of the disease. The ganglia on the posterior roots seem to offer an impassable barrier. Experimentally a very painful form of the disease—tetanus dolorosa—was produced by injecting the toxins into the posterior roots on the proximal side of the ganglia. In this form of the disease there were none of the characteristic motor phenomena; the animals died probably from exhaustion attending the excruciating paroxysms of pain.

The conclusions to be drawn from these experiments are rather that the toxins are not deposited in the cord directly from the circulation but always through the medium of the motor nerves. The real significance of these observations will be more fully realized when they are applied to the question of prophylaxis and treatment.

To recapitulate, it has been determined that the toxins are taken up by the motor nerves and only by them, and carried directly to the spinal cord.

It remains now to consider the effect of the toxins upon the structure and formation of the cord. In the first place, it may be said that the motor tracts of the cord are those chiefly affected; the toxins are carried by the motor nerves and deposited in the motor ganglia; from these they spread upward from one segment of cord to another, but not to the sensory tracts. If the cord is divided between the lumbar and dorsal segments the progress of the toxin will be prevented and the manifestations of tetanus limited to that section supplied by the lumbar segment. To further prove the means of transmission it has been shown that subdural injections of the toxin do not affect the cord directly; they may find their way into the general circulation and eventually through the medium of the nerves reach the end and cause tetanic symptoms.

What is the physiologic action of the toxins upon the nervous system? The answer to this question will explain the symptomatic expressions of tetanus. Tetanus is essentially a disease of the spinal cord and medulla; decapitation of an animal will in nowise interfere with the clinical expressions of the disease. (Experimentally, however, there is a form of tetanus which Roux and Borrel [34] called cerebral tetanus. This form of tetanus was produced by the injection of the toxins directly into the brain and was characterized by a train of symptoms which were chiefly psychic and not at all like those which we commonly associate with the usual type of tetanus.) Whatever may be the structural changes in the cord, the specific action of the toxins is the production of a condition of hyperexcitability of the motor ganglia which accounts for the tonic contractions. The clonic contractions are the result of reflex excitability. Archibald [35] gives a very excellent résumé of the views of Meyer and Ransom upon this subject: "At the point of inoculation the toxin is sucked up largely by the motor nerves, in all probability by their bared axis-cylinder endings from the lymph spaces; and is by this path transported to the motor ganglia of the cord. These are at first only put into a condition of hyperexcitability, so that they are aroused by the stimuli which are continually streaming in from the sensory periphery, and which ordinarily remain latent so far as exciting motor action is concerned. These stimuli are now sufficient to cause a continuous discharge of energy much greater than the ordinary, sufficient, indeed, to bring the muscle into contraction. First the extensors and flexors both become slowly and moderately tense; but gradually the extensors overcome the others and extend the leg fully,—the so-called extension cramp. Local tetanus is thus the expression and the consequence of the normal muscle tone, but so increased that it overcomes all central inhibition.

"The pathologic substratum is an irritation of the motor apparatus in the cord, and therefore it remains at first localized. The extra toxin is carried on in the fibers of the cord, at first by way of the direct association fibers through the anterior commissure to the motor apparatus of the other side, causing tetanus of the corresponding limb. Only after some time and with a sufficient import of toxin does the latter take hold of the tactile apparatus of the reflex arc, the nearest associated part of the nervous system, producing reflex hyperexcitability. Thus it comes to general tetanus of the reflexes. A stimulation of the involved limb or its nerve root will cause an abnormally severe motor explosion, which can spread by ascending and descending collaterals to the reflex apparatus of the whole cord; and, conversely, upon stimulation elsewhere, the transmitted wave causes a reflex jerk, only in the hyperexcitable district. If the toxin spreads, both motor hypertonus and hyperexcitability spread also, and we get stiffness of almost all voluntary muscles together with general reflex hyperexcitability.

"Thus there are two separate processes going on in the cord. The first is a local motor poisoning resulting in local tetanic muscle spasms; the other, secondary, is local sensory poisoning, a reflex tetanus spreading from the poisoned neurone."

Varieties of Tetanus.—Tetanus may be classified as acute, subacute, and chronic, as idiopathic or traumatic. Although the period of inoculation is very variable, the symptoms of acute tetanus usually appear about the end of the first week and the disease runs a comparatively rapid course. Traumatic tetanus is by far the commonest form; idiopathic tetanus, developing without sign or history of an injury, may be due to the inhalation of the tetanus bacillus in dust or its ingestion in contaminated new vegetables. If any sharp line was drawn for purposes of classification the acute cases may be said to be those which develop in less than ten days, the subacute those in which the period of incubation is ten days or longer. The term chronic tetanus applies rather to the duration of the disease than to the period of incubation. The symptoms persist for months or even years.

Tetanus neonatorum, or **trismus nascentium,** is a form of tetanus in the new-born, in which the infection takes place through the navel. It differs in no way etiologically from the other forms of tetanus, begins as in the other forms with trismus and spreads to the other muscles. In maternity obstetric wards or hospitals it occurs in epidemic form. The introduction of antiseptic methods in the treatment of the stump of the umbilical cord has practically eliminated the epidemic type of the disease.

Cephalic tetanus or **tetanus hydrophobicus** is a form of tetanus complicating injuries in the distribution of the cranial nerves and involving the muscles supplied by these nerves and occasionally muscles of the trunk. Paralysis of the facial nerve, trismus, and spasm of the pharyngeal muscles are the most common symptoms.

Experimentally there are two forms of tetanus: *cerebral tetanus*, which follows the injection of the toxin into the brain and is characterized chiefly by psychic disturbances, and *tetanus dolorosa*, which occurs after injection into the posterior roots of the spinal cord. It is attended with excruciating pain in the distribution of the nerve without any muscular phenomena.

Immunity and Prophylaxis.—This leads us at once to the discovery of antitoxin. Although prior to this time a number of experiments had been carried on with a moderate degree of success, it was not until 1890 that Behring and Kitasato [36] proved conclusively that under the protection of an antitoxin animals could enjoy an immunity against the toxins. The experiments which led up to their discovery of the antitoxin proved that there was present in the blood-serum of artificially immunized animals a substance which, when mixed with a virulent culture of tetanus bacillus, destroyed its poisonous qualities. In the following year these results were confirmed by Tizzoni and Cattani,[37] and the nature of the antitoxic substance was found to be an enzyme. A year later Behring [38] began his work in the immunization of large animals, particularly the horse, and since that time the horse is used in the manufacture of the commercial antitoxin. While it is known that antitoxin has both an immunizing and to a certain extent a curative power, the precise mode of its action is a matter of discussion. Behring and Kitasato regarded the action as a purely chemical one, in which the antitoxin actually neutralized the toxin. Their experiments, made with the test-tube and not in the human subject, were disproved by Buchner.[39] According to the latter's theory, these two substances—the toxin and the antitoxin—do not act directly upon one another, but only through the medium of the living body. Finally the side-chain theory of Ehrlich has been made use of to explain the action of the antitoxin and has received support from many observers.

After the antitoxic substance is injected into the tissues it is taken up so slowly that the maximum amount is not found in the circulation until the end of twenty-four to forty hours. The greater portion of it is eliminated unchanged in the secretions and excretions, such as the milk, feces, and urine. So far as we know, the antitoxin is not taken up at all by the nervous tissues, and even after injections of large quantities there will be but a trace found in the cerebrospinal fluid. At the end of a week there will be only one-third of the original amount, and in three weeks the entire amount will have disappeared. The antitoxin does not destroy the toxin, but through some chemical process renders it inert. These few facts, with reference to the behavior of antitoxin after its injection into the tissues, have a most important practical bearing as to the method of administration and as to the results which should be anticipated. (1) Owing to the fact that absorption takes place so slowly the injection should be made directly into a vein. (2) Inasmuch as a greater portion of antitoxin is eliminated unchanged, the injections must be repeated sufficiently frequently to make up for the continuous loss. (3) The inability of nervous tissues to take up the antitoxin from the circulation is the most significant fact of all. It shows the futility of subarachnoid injections, it reminds us that subcutaneous or intravenous injections are only of value in so far as they can neutralize the toxin circulating in the blood, but cannot influence the process in the spinal cord, and it suggests the only rational method of administration, when combating the disease, namely, intraneural and intraspinal injections. The dangers of delay and, especially, the importance of prompt action are forcibly illustrated by the results of animal experimentation. Thus, two minutes after an injection of a fatal dose of toxin, twice as much antitoxin is required as would have been necessary had the antitoxin been administered simultaneously; after the lapse of eight minutes, ten times the amount of antitoxin is required; after ninety minutes, forty times the amount, and so on. To protect an animal from experimental tetanus the antitoxin must be administered not less than twenty-four or more than forty hours before the administration of the toxin (Rogers[10]). When considering the dosage in an individual case it should be remembered that tetanus antitoxin is entirely harmless and that it is much safer to give too much than too little.

The protective power of tetanus antitoxin both for animals and man has been settled beyond a doubt. The tetanus bacillus generates its toxin so rapidly and so minute an amount is necessary to precipitate a fatal attack that it is all-important that the precautionary measures should be executed with celerity. So rapid is the train of events that the danger may be said to increase at least with every hour, if not with every minute of the hour. Simultaneously with the disinfection of the wound, an immunizing dose of antitoxin should be administered into the tissues about the wound. Owing to its slow absorption, if injected subcutaneously, Rogers recommends the intravenous method. If the tetanus bacillus is found in cultures taken from the wound, the antitoxin should be given immediately and repeated daily until at least two weeks have elapsed from the time of the receipt of the infection. Ten to 20 c.c. of the antitoxin should be injected directly into a vein, such as the median basilic, and into the tissues around the infected region. In veterinary practice, where the prophylactic use of tetanus antitoxin has been so successful, the injections are made subcutaneously.

Antitoxin has been used with great frequency, or at least more consistently, as a prophylactic measure with horses than with man. Nocard[40] tested the efficacy of this remedy on a very large scale. He distributed 7000 immunizing doses of his antitoxin to veterinarians with instructions that two injections should be given at intervals of ten or twelve days. Of 2700 cases in which these instructions were carried out, there was not a single case of tetanus developed. On the other hand, there were 259 cases of tetanus reported to him as developing in animals not injected. Of 163 castrations performed on horses receiving the antitoxin, not one developed tetanus, whereas in a series of eight cases unprotected by the antitoxin tetanus developed in five. Statistics of the same convincing nature could be quoted from many other sources. It is a more difficult matter to determine the effect of prophylactic doses in man. The disease is not quite so prevalent in man as in horses, and there is not as much likelihood of tetanus developing in neglected or unprotected cases. Judging, however, from the experience of those who have had the opportunity to test its efficiency, we are warranted in recommending the use of tetanus antitoxin as positively for man as for animals. In a special investigation made by the authorities of the "Journal of the American Medical Association" they were unable to discover a single case in which a person who had received the antitoxin subsequently developed tetanus.

An immunizing dose should be administered in every suspicious case, and the dose should be repeated on the third, fifth, and fifteenth to twentieth day. It is necessary to repeat the dose because the protective influence of the antitoxin lasts only a few days. Suter (Jacobson[57]) reported a case in which the disease developed forty-seven days after a prophylactic dose had been given, and collected 110 other cases, to which Jacobson has added six. The injection should be made directly into the muscle tissue because from here absorption is more rapid.

In addition to the administration of the immunizing dose of antitoxin, every suspicious wound should be thoroughly disinfected after a culture has been made. This disinfection to be effective must be radical, and should be done under a general anesthetic. The wound should be laid open throughout its entire length, if possible, all dirt and necrotic tissue should be removed, and the entire wound surface disinfected and continuously bathed in one of the following solutions: 1.5 per cent. carbolic acid solution, a 1:1000 nitrate of silver solution, or a 1 per cent. iodin trichlorid solution. The iodin and carbolic acid solutions are to be preferred. On account of the iodin contained in it, iodoform gauze may be used for subsequent dressings. The use of the actual cautery or strong caustic substances, as, for example, pure carbolic acid, is not to be recommended, because the eschar which forms over the wound surface will prevent the oxygen of the air reaching the tissues and thus bring about conditions favorable to the growth of the organism.

McFarland,[41] in an experimental study, found that antitoxin in the form of a dry powder was very effective in the treatment of wounds. After dusting the wound with this dry dusting-powder, tetanus failed to develop in every case, even after a drop of the pure tetanus culture had been vigorously rubbed into the abraded surface. He recommends the systematic employment of this powder in the dressing of all suspicious wounds; it preserves its activity indefinitely, can be conveniently sprinkled from the bottle in which it is dispensed, it is devoid of irritating property, when applied to a wound surface it acts not only by neutralizing the toxin, as it is elaborated in the wound, but also the toxin in the circulation. It is needless to say that one of the most efficient prophylactic measures, at least in this country, is the enactment and enforcement of laws regulating the use of explosives on the Fourth of July, especially the toy pistol and cannon cracker. Blank cartridge wounds are most deceptive; on the surface they present rather a clean-cut wound, but owing to the explosive nature of the cartridge the principal damage is beneath the skin. By the force of the explosion the powder and dirt may be found at a considerable distance from the wound.

Incidence.—Tetanus is endemic to all large centers of population, and there are certain districts where it appears to be especially prevalent. In certain instances, as in maternity hospitals, tetanus, in the form of tetanus neonatorum, may be said to be epidemic. In Great Britain between 1892 and 1897 there were 3537 deaths from tetanus, 2969 of which were directly traceable to traumatism (quoted from Symmers[42]). According to Anders,[43] who has made a statistical study of all cases in the United States from 1850 to 1904 that could be gathered from literature or by correspondence, tetanus is most prevalent in northern New York, along the Hudson Valley, in Brooklyn, Long Island, southern Pennsylvania, Virginia, Georgia, southern Louisiana, Indiana, Illinois, and southern California. Out of 1201 cases, collected by Anders, Pennsylvania led with 224, and New York came next with 190. There is a strip of land in New Jersey about five miles long and a mile wide where tetanus is said to be markedly endemic. The extremities are the most common seat of infection, especially the hands and feet, and males are more susceptible than females.

While the majority of the cases of tetanus are due to punctured wounds, a very considerable number are associated with lacerated wounds, and a few have been recorded complicating operations. In an analysis of 78 cases collected by Jacobson[57] it was found that 52 were the result of wounds inflicted by blank cartridges or gunshot wounds, and 26 cases complicated lacerated wounds. In this same series one case is reported as developing six days after a supravaginal hysterectomy and double oöphorectomy, another as following an operation for varicocele by an "advertising" doctor, and another, occurring in the Göttingen clinic, as following a Bassini operation. The latter case was attributed to the fact that a case of tetanus had been treated in the clinic on the day prior to this operation. In addition to these, Jacobson found five cases following operations performed under aseptic conditions upon the intestines, four for the removal of the appendix in the quiescent period, and the fifth a colectomy for the removal of the splenic flexure.

Fourth of July Tetanus.—A large percentage of cases in the United States are directly attributable to the accidents occurring during Fourth of July celebrations. In 1903[44] there were 415 cases of tetanus due to Fourth of July injuries. In 1904 there were but 105 cases. Whether this striking falling-off in the number of cases was due to the fact that the tetanus bacillus was not so prevalent, or whether it was due to the efforts which were made by the medical and lay press to educate the laity and compel the authorities to enforce the laws restricting the sale of explosives, is a matter of conjecture. As a result of Fourth of July injuries in 1903 there were 406 deaths from tetanus, as compared with 60 from all other sources; and of these, 363 were due to blank cartridges, 29 from all other known causes. There were but 7 recoveries, making the mortality well above 95 per cent. The damage to the tissues as the result of the explosion offers a very fatal field for the tetanus bacillus. The majority of cases are due to toy pistols, but the wounds made by giant and cannon crackers are especially favorable for tetanus bacilli when there is much laceration and burning of the flesh.

ACUTE TETANUS.

Symptoms.—The incubation period of acute tetanus is about seven to ten days. This comparatively long period of incubation has always been a puzzle until the recently advanced theories as to the part played by the nerves in the transmission of the toxins to the spinal cord. The time intervening between the date of infection and the date of the initial symptoms is the time required for the toxin to travel from the motor nerve-endings to the cord. Thus the shorter the nerve, the shorter the period of incubation. Thus if we compare the period of incubation in animals, whose peripheral nerves vary in length, we find that the period of incubation in the mouse is eight to twelve hours; in guinea-pigs, thirteen to eighteen hours; in rabbits, eighteen to thirty-six hours; in the cat, twenty-eight to seventy hours; in the dog, thirty-six to thirty-eight hours; and in the horse, five days. That the period of incubation has nothing to do with the susceptibility of the horse is evident from the fact that of these animals the horse is more susceptible than the majority of others. In further confirmation of this explanation attention is called to the fact that the period of incubation is not shortened even when the tetanus toxin is injected into the subdural or subarachnoid space. Before reaching the spinal centers it must enter the circulation and be carried to the motor nerve-endings. In man the first symptoms of the disease appear almost invariably without any reference to the seat of the disease, with the exception, perhaps, of cephalic tetanus, in which the muscle phenomena are confined to the distribution of the cranial nerves. Experimental tetanus differs from human tetanus in that the disease is at first a local one, involving only the limb in which the toxin was injected.

The first symptom in man is stiffness of the muscles at the back of the neck, sometimes preceded by a chill. In the course of a few hours owing to the rigidity of the masseter muscles the jaws become rigid (trismus or lock-jaw). The constancy with which trismus appears as one of the initial symptoms has been attributed to the fact that the fifth nerve, besides being a short one, seems to be unusually susceptible to the tetanus poison. After the masseter the other muscles of the face and jaw and the muscles of deglutition become affected. Spasm of the latter cause great difficulty in swallowing even liquids and the accumulated mucus in the throat. The nostrils are raised and the mouth puckered in such a way as to give the patient that peculiar expression known as the risus sardonicus. The eyebrows are contracted, the eyes drawn in and partially closed, and occasionally there is strabismus. Next to the muscles of the neck and face the muscles of the trunk are involved; the abdominal muscles become rigid and as "stiff as a board," and soon afterward the muscles of the back. Finally the disease attacks the muscles of the extremities, especially of the lower extremity. There are two muscular phenomena—the tonic and the clonic contractions. The former, as the term implies, cause constant rigidity, while the latter, which are paroxysmal in type, are represented by convulsive seizures which are usually attended with a great deal of pain. These paroxysmal seizures are precipitated by the most trivial causes, such as a slight noise, a jar of the bed, or even a draught of air. They occur with variable frequency every few minutes, almost incessantly, or only once in several hours; they are followed by profuse diaphoresis, and contribute greatly to the patient's suffering and ultimate exhaustion. The attitude of the patient is quite characteristic. Owing to the rigidity of the muscles of the neck and back, the head is drawn back and the spine arched. If he is lying on his back during one of the paroxysmal seizures, the back and legs will be so arched that the only two points in contact with the bed will be the back of his head and his heels (opisthotonos); if on his side, only the side of his face and leg (pleurothotonos); or if on his face, only his forehead and toes (emprosthotonos). Owing to the involvement of the muscles of deglutition, the patient can swallow nothing but liquids; in fact, nothing else can be introduced through the locked jaws. The rigidity of the muscles of the mouth and throat so interfere with articulation that the patient in an attempt to speak can only utter a muffled groan or a cry. Evacuation of urine and feces is difficult because of the rigidity of the sphincters.

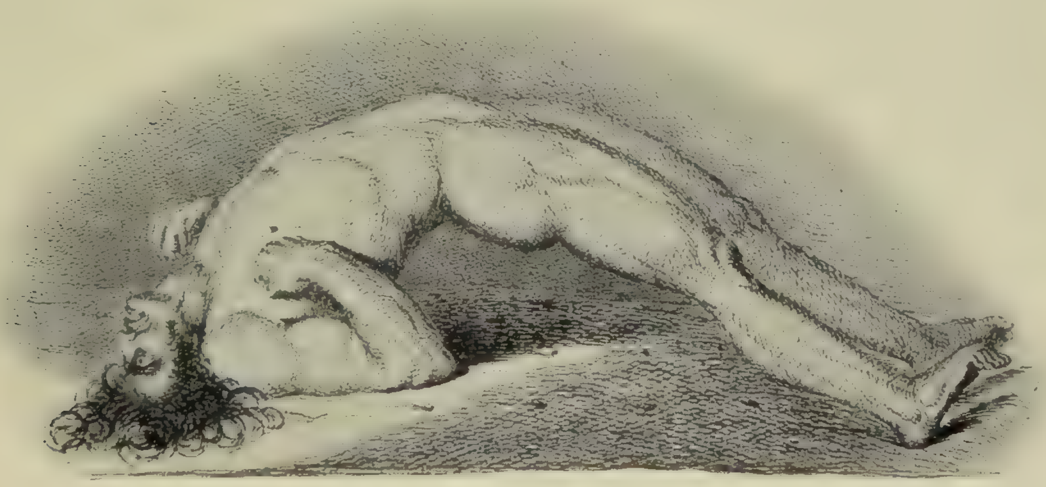

FIG. 133.—OPISTHOTONOS (Bell).

The patient's condition is rendered all the more distressing because his mind is always so clear that up to the end he is sensible of the agony of the disease. To contribute further to his suffering, he is often denied the relief to be derived from sleep, unless the convulsions respond to the treatment. As a rule, the temperature is little if any elevated until just before or after death, when in some cases it rises to 105° to 110° F. The pulse becomes more rapid as the disease progresses and the respirations become embarrassed by the involvement of the respiratory muscles. The face is pale and emaciated and the expression anxious. Pain is not a characteristic feature of the disease, except as it accompanies the convulsions; then it is agonizing.

Chronic Tetanus.—The symptoms of chronic tetanus may appear in the same order as in acute tetanus, and while the convulsions may be quite as severe, the intervals between the convulsions are longer. The patient may be enabled to enjoy periods of prolonged and refreshing sleep denied him in the acute form of tetanus. Chronic tetanus is characterized often by periods of relapse, so that the disease may persist for a considerable time. Grober[58] reported a case in which the patient had apparently recovered from a typical attack of tetanus and a month later the symptoms recurred, although there had been no new source of infection. Tonic spasms developed in the muscles of the arms, thighs, and jaws.

Secondary contractures have been noted as sequels of chronic tetanus. Thus in Grober's case even two years after the onset the teeth could not be separated more than 5 cm. In Damascus and Beirut, Brun[59] saw three cases in which after a prolonged convalesence these sequels were noted. There were contractures in the muscles of the extremities and jaws, noted three months, four months, and five years respectively after the onset of the disease. These contractures are due probably to a chronic fibrous myositis. The prognosis is not good, but the condition may be alleviated by warm baths, electricity, and exercise.

Diagnosis.—The diagnosis of acute tetanus is not, as a rule, attended with any difficulty, except perhaps in its early stages. Parotitis, tonsillitis, inflammatory affections of the mouth or cervical nodes, or an arthritis of the temporo-maxillary articulation may cause stiffness of the neck and jaws, but here the similarity ends. The tetanus spasms following the dressing of a painful wound, and the hysterical contraction of the masseter muscles, should be easily differentiated. Peripheral irritation of scars or foreign bodies has given rise to tetanic spasms which in some instances terminated fatally. The conditions with which it is more likely to be confounded are strychnin poisoning and hydrophobia. In strychnin poisoning there may not be the associated wound, trismus is not the earliest sign, the muscles of the extremities and trunk are more seriously affected than those of the face, and there is not the persistent rigidity between the spasms. Laryngismus is characteristic of strychnin poisoning, as is also hyperesthesia of the retina and misperception of color, all objects appearing green. In hydrophobia there is always the history of a bite by a rabid animal, the individual paroxysms are more distinct, are limited to the muscles of respiration, and are followed by periods of relaxation; the mania is a distinctive feature.

Tetany is a very much rarer disease, occurring chiefly in young people, is characterized by convulsions, tonic contractions in groups of muscles, especially of the upper extremity. The convulsive attacks are intermittent, and between the attacks the patients are entirely well. Tetany follows thyroidectomies, puerperal fevers, or mental shock; it is due to hyperexcitability of the gray matter of the cord and medulla, and has this diagnostic feature, namely, that pressure upon the nerve-trunk supplying the affected muscles always precipitates an attack (Trousseau's symptom). Tetany is not a fatal disease.

In cerebrospinal meningitis there is the stiffness of the muscles of the back and neck, as seen in tetanus, but these cerebral symptoms are in themselves sufficient to distinguish it from tetanus. When the opportunity and facilities are offered, cultures should be made as a routine practice from those wounds which, as a class, predispose toward tetanus.

Prognosis.—Generally speaking, the prognosis of tetanus depends upon whether the disease manifests itself as of the acute, subacute, or chronic variety. Acute tetanus has been one of the most fatal of diseases, but the longer the patient lives, the greater the chances of recovery, as a majority of the fatal cases die before the fifth day. In a series of cases collected by Anders[43] the highest mortality occurred on the seventh day. There were 338 cases with a mortality of 275, or 81.4 per cent. in cases lasting five days or less; there were 231 cases with a mortality of 144, or 63 per cent., in cases lasting five to ten days; and in those lasting from ten to fifteen days there were 91 cases with 27 deaths, a mortality of 30 per cent. If we regard as acute tetanus those cases developing within ten days, the mortality was 74 per cent.; of those lasting over fifteen days, the mortality was but 8.5 per cent. The following is the table prepared by Anders showing the relation of the mortality to the duration of the disease:

	CASES.	RECOVERY.	DEATH.
Less than one day	7	1	6
One day	47	9	38
Two days	79	8	71
Three days	71	13	58
Four days	66	16	50
Five days	68	16	52
Six days	35	8	27
Seven days	86	30	56
Eight days	33	9	24
Nine days	25	9	16
Ten days	51	30	21
Ten to fifteen days	91	64	27
Fifteen to twenty days	46	41	5
Twenty days and over	165	152	13
Totals	870	406	464

Jacobson[57] has recently prepared very elaborate statistical tables showing the mortality of tetanus in a series of 203 cases. These statistics are infinitely more valuable than any hitherto presented because they exclude individual cases or series of cases reported at random (which usually are the successful ones) and are composed of all the cases treated by a large number of selected hospitals or individual surgeons. If we turn to these (see below), it will be seen that the average mortality in all acute cases was 83.1 per cent., and in all subacute cases was 43.6 per cent., or an average for both of 63.3 per cent.; that the lowest mortality in the acute cases was 79 per cent. and occurred in a series of cases treated by subcutaneous injections; the highest mortality in acute cases, 93 per cent., occurred in a series of 48 cases treated by various combinations of intravenous, subcutaneous, intramural, intraspinal, and intracranial injections. The average mortality in those cases treated with antitoxin serum supplied by the New York State Department of Health was lower than when the antitoxin came from other sources. It would appear from these statistics that in the active treatment of tetanus the antitoxin had been of somewhat doubtful value, no matter how administered. However, it is only quite recently that we have discovered the means by which the toxins reach the cord. The last word as to the efficiency of serum therapy as applied to tetanus should not be spoken until a very thorough trial has been given the intraneural injections. The failures of the past may be attributable rather to faulty technic than to the inefficiency of the serum. Above all is the prognosis influenced by the early recognition of the disease and the immediate adoption of suitable remedies. In the treatment of no other disease is time so important an element.

Jacobson's Statistics.—In these tables acute cases imply those with an incubation period of less than ten days, subacute cases with an incubation period of ten days or longer.

Table I includes cases treated with antitoxin from other sources	144 cases.
Table II includes cases treated with New York State Department of Health antitoxin	159 cases.
	303 cases.

Table I.		Table II.
66 cases	treated by subcutaneous injections	42 cases.
48 "	" " injections into various structures	16 "
12 "	" " intraspinal injections	—
16 "	" " intramuscular injections	—
1 case	" " intracerebral injections	1 case.
1 "	" " intravenous injections	—
144 cases.		59 cases.

Table I.	Mortality.
93 acute cases	85.7%
44 subacute cases	34.9%

Table II.	Mortality.
29 acute cases	80.6%
21 subacute cases	52.4%

Table I.		Mortality.
66 subcutaneous injections,	47 acute cases	82.6%
	18 subacute cases	22.2%
48 cases, combination of intravenous, subcutaneous, intraneural, intracranial, and intraspinal injections,	30 acute cases	93%
	14 subacute cases	50%
Intraspinal injections, 12 cases,	7 acute	57%
	3 subacute	

Table II.		Mortality.
Subcutaneous injections,	24 acute cases	79%
	16 subacute cases	43%
Injections into several structures,	11 acute cases	81%
	5 subacute cases	80%

Therapeutic Considerations.—Bacelli's Carbolic Acid Treatment.—In 1888 Guido Bacelli, of Rome, presented to the Italian Congress of Internal Medicine his plan of treating tetanus by the subcutaneous injection of carbolic acid. Prior to that time Bacelli [46] had observed the tolerance to carbolic acid of patients suffering from neuralgia; having treated some 600 cases with such beneficial results, he determined to try the effect of the carbolic acid injections upon tetanus. As an antiseptic, as an analgesic, as having the property of diminishing reflex activity in the spinal cord, as having an almost specific effect in inhibiting the growth of the organism and neutralizing its toxins, carbolic acid was pronounced to be a valuable remedy in the treatment of tetanus. As an argument against its use it has been claimed that it coagulates the albumin in the tissues, and is therefore very slowly absorbed, and when absorbed is rapidly eliminated. In answer to this, it is claimed that dilute solutions are incapable of coagulating albumin, but retain their antidotal effect upon the tetanus toxin. The extraordinary tolerance of the human subject to large doses is attributed to the fact that carbolic acid is rapidly eliminated, and a portion of it may enter into chronic union with the toxin (Symmers [42]). Sixty to eighty grains (4 to 5 grams) may be administered with impunity to a tetanus patient in one day. It has been claimed for the Bacelli treatment, that since carbolic acid is always available, the treatment can be instituted without delay, and that its employment does not prevent the use of the antitoxin or any of the nervous sedatives. The soluble sulphates and alcohol are contraindicated. The treatment consists in the subcutaneous injection of a 1 per cent. solution of carbolic acid until 80 grains, or 5 grams, are given to an adult in twenty-four hours. Owing to its rapid elimination, the injections should be given at short intervals. As to the results, it may be said in general that, outside of Italy, where the method is most popular, the results have not been very convincing. Of 33 cases collected by Ascoli,[47] there was but one death, a mortality of 3.3 per cent.; but in the 42 cases tabulated by Symmers,[42] there were 16 deaths, or a mortality of 38.1 per cent.; or, combining the two tables, there were 75 cases with 17 deaths, a mortality of 22.6 per cent.

Serum Therapy.—Years have elapsed since Behring announced to the world his discovery of the tetanus antitoxin. Brilliant as have been the results following its use as a prophylactic, as a curative agent the results have been most disappointing. How it suffers when compared, for example, with what has been accomplished by the diphtheria antitoxin! The great disparity between the effects of the administration as a prophylactic and as a curative agent is easily explained by the great affinity of the toxins for the cells of the spinal cord, on the one hand; on the other, by the inability of the nervous tissues to take up the antitoxin. But, as has been said, the long list of failures may be due to faulty technic rather than to the inefficiency of the antitoxin. The great trouble has been that up to within a few years men were working more or less in the dark, because they did not understand, what has since been demonstrated, that the toxins reach the cord only through the motor nerves. Even when working under such disadvantages the profession has been able to reduce the mortality by the use of antitoxin. It is no longer a question as to whether the antitoxin should be used, but only how it should be administered.

Up to within two years ago there were but four methods—the subcutaneous, the intravenous, the intracerebral, and the subarachnoid. The subcutaneous method has certain disadvantages which have already been referred to, chief among which is the slowness with which the serum is absorbed. In most cases in which time is an important element the intravenous method should be preferred, since it brings the antitoxin immediately in contact at least with the toxin in the blood. In neither the subcutaneous nor the intravenous method is the antitoxin brought into contact with toxins in the spinal cord.

In 1898 Roux and Borrel [48] introduced a modification of the technic, which consisted in injecting the antitoxin directly into the brain. Knowing the inefficiency of the antitoxin, if injected subcutaneously when the cells are already saturated with toxin, it was thought that by direct injection into the brain a fatal issue might be prevented if the virus had not yet reached the vital centers of the cord. Their experiments seemed to prove that, injected in this way, the upper portion of the spinal cord could be protected. This idea proved popular with the profession, and from 1898 to 1902 or 1903, Roux's intracerebral method was widely practised. In referring to the statistics (which must always be unreliable when composed chiefly of individual observations, because the favorable cases more often find their way into literature than the unfavorable) we find that Lambert [9] quotes a mortality of 63.46 per cent. in a series of 52 cases; the mortality of the acute cases was 87.5 per cent. and of the chronic 26.66 per cent. Schauffler [49] collected 233 cases with a mortality of 58 per cent. Of 48 cases in the series of Moschowitz [50] there was a mortality of 52.88 per cent. Though it would appear from these statistics that the mortality had been reduced by this method, it is difficult to understand the rationale of injecting the antitoxin into the brain, when the toxin acts almost exclusively upon the cord and medulla. Cognizance should be taken of the fact that in many of these cases both intravenous and subcutaneous injections were given simultaneously with the intracerebral injections.

In 1898 Jacobs [52] recommended the subarachnoid injection of antitetanic serum in the belief that the serum would be brought more promptly into contact with the affected cells of the spinal cord. According to our modern conception of the pathology of the disease, there is no reason to believe that the presence of the antitetanic serum in the subarachnoid space will have any effect upon the toxin within the cord. This method has, therefore, nothing to recommend it, and is simply mentioned to make the historical record complete. Symmers [42] collected 31 unclassified cases treated by Jacobs's method with a mortality of 32.35 per cent., and of the ten fatal cases three were in infants, in which class the disease is extremely fatal, and three succumbed to pneumonia, the tetanic symptoms having entirely subsided in two. From 1898 to 1903 there were no especially important contributions made having any direct bearing upon the serumtherapy. In this year Meyer and Ransom [32] published their work proving experimentally their "motor nerve path" theory of the transmission of the toxins to the cord. In the course of their experiments to substantiate their theory they found that by injecting the sciatic nerve of a cat, six hours after the introduction of a lethal dose into the jugular vein, that while the animal died, both hind-legs remained free from tetanic convulsions. When the toxin was introduced into an extremity they were able to protect that extremity from tetanic convulsions by blocking the nerve with antitoxin. It was not long before the clinician took advantage of these experimental results. Rogers [51] was the first to apply these experimental results to the treatment of tetanus to man, and his contribution marks the last step in the history of the serum-therapy. In a series of seven cases he injected the serum subcutaneously, intravenously, intraneurally, and into the lumbar cord, and in three cases he even injected the antitoxin into the cervicodorsal segment of the cord. Of these three cases one recovered, one succumbed after a relapse, which was attributed to a mistake whereby diphtheria antitoxin was given instead of the antitetanic serum, and the third died without any relief. Of the remaining cases, all survived but one. Rogers's plan of treatment consists in the injection of 10 to 20 c.c. subcutaneously in the neighborhood of the wound, of 10 to 20 c.c. intravenously, with the injection of 5 to 20 minims into the nerves of the axillary plexus, if the wound is in the upper extremity, or into the crural, sciatic, and obturator nerves if the wound is in the lower extremity. In addition to this, he injects 10 to 20 c.c. into the nerves of the cauda equina; and if the patient's life is in imminent danger, in order to protect the vital centers of the respiration and circulation, 20 to 30 minims are injected directly into the cord between the sixth and seventh cervical vertebræ. Realizing the danger of a procedure involving hemorrhage into the cord, he noticed absolutely no ill effects. In addition to those of Rogers's series, another successful case has been reported by Clairmont.[53] In this case 200 units were injected subcutaneously and 100 units injected into the stump after the limb was amputated.

Injection of Brain Emulsion.—Based on the principle that brain tissue has an especial affinity for tetanus toxin as demonstrated by Roux and Borrel,[48] Krokiewicz [54] recommended the subcutaneous injection of an emulsion of fresh brain tissue in the treatment of tetanus. It was found that, if the brain emulsion was shaken up with tetanus toxin, upon standing the toxins would all be removed from the supernatant fluid and combine with the brain tissue in a harmless form. Using the brain of a freshly killed dog, rabbit, or sheep, an emulsion is prepared by adding 10 to 15 grams (½ ounce) to about 30 c.c. (1 ounce) of sterile salt solution. This solution is to be strained through sterile cheese-cloth under slight pressure and injected subcutaneously, in the neighborhood of the wound, if possible. The injection should be repeated every other day, or every two or three days, according to the severity of the disease. Krokiewicz has collected 16 cases of traumatic tetanus which were treated in this way, 13 of which recovered, and 8 of these were cases of more than average severity. It may be said of this method of treatment that it is entirely harmless and does not contraindicate the use of antitetanic serum. The treatment seems to be more popular in Russia than in any other country.

Injection of Salt Solution.—Matthews[55] advocates the injection of a solution of the following ingredients:

Sodii chloridi	gr.	55.5	7	3125
" sulphatis	gr.	155	10	06
" citratis	gr.	51	3	364
Calci chloridi	gr.	2	0	136
Aquæ	pints	2	1000	00

The solution should be injected directly into the venous circulation, and so slowly that not more than 3 c.c. passes into the vein every minute. The efficacy of this solution is due partly to the calcium chlorid in lessening irritation and partly to its diuretic effect, which insures the rapid elimination of the tetanus toxins. Matthews has applied this treatment with positive results, especially in the case of a boy whom he saw on the ninth day of the disease. On the twelfth day the boy's condition was alarming, his pulse was 150 and his temperature 105° F. In two and a half hours he injected 600 c.c. of the special salt solution, and during the injection the pulse fell to 104 and remained there until the following afternoon, when it rose to 140, the convulsions at this time threatening the patient's life. Upon the repetition of the injection the pulse dropped to 98 and a large quantity of urine was excreted. The following day it went up to 130 and dropped under the treatment to 94. No further treatment seemed necessary and the boy continued to improve from that time on. Two cases are referred to,[44] one of which recovered under this treatment; the other was on the road to recovery, but died of aspiration pneumonia.

Subdural Injections of Morphin-eucain and Salt Solution.—Murphy[56] recommends the withdrawal of some cerebrospinal fluid and the injection of a morphin-eucain solution. He employed this treatment in one case with satisfactory results; $\frac{1}{75}$ of a grain of morphin and $\frac{3}{50}$ of a grain of eucain were introduced with each injection, and immediately afterward the spinal muscles relaxed, and remained so for a considerable period of time. Immediately after the first injection the patient slept four hours. Three c.c. of the solution were introduced into the subarachnoid space after withdrawing 16 c.c. of cerebrospinal fluid. On the following day 4 c.c. of the above solution was injected, after the withdrawal of 15 c.c. of cerebrospinal fluid, and on the following days 15 c.c. of fluid was withdrawn and 4 c.c. of the solution was injected. The patient's condition continued to improve, so that but one more injection was necessary. The effects of this treatment, according to Murphy, are to be attributed either to the extraction of the cerebrospinal fluid, or to the injection of the eucain solution, or to both. From our recent knowledge of the pathology of tetanus, it does not seem reasonable to attribute any benefit to the withdrawal of the cerebrospinal fluid, since the toxins are only found in the cerebrospinal fluid after the injection of massive doses, and then only in small quantities. The condition of the cerebrospinal fluid in no way influences the progress of the disease. Attention has already been called to the fact that the injection of the toxins directly into the subarachnoid space cannot reach the cells of the cord until it is taken up by the circulation, and deposited in the muscles. In the case reported by Murphy the effect of the injections of eucain-morphin upon the symptoms was so prompt and positive that, even though the rationale of the treatment may not be thoroughly understood, this possible means of relief must not be lost sight of, particularly in cases in which the patient is becoming exhausted by the frequency and severity of the convulsions.

Subdural Injections of Magnesium Sulphate.—Quite recently magnesium sulphate has been added to the list of remedies for the treatment of tetanus. S. J. Melzer called attention to the inhibitory effect of the drug upon both afferent and efferent impulses when applied to nerve tissues. At the present writing, according to Blake,[60] but four cases have been treated with this remedy, two by Logan,[61] one by Markoe, and one by Blake,[62] the latter's case being the only one of the four to recover. The drug is in no sense a specific for tetanus, but by its physiologic action it may inhibit the convulsive seizures, and by so doing relieve the exhausting effects of both convulsions and pain. When injected into the subdural space of the lumbar region the drug produces paralysis both of motion and sensation, at first in the lower extremities, and afterward in the trunk and upper extremities. Inasmuch as magnesium sulphate has a depressing effect upon the higher centers, both in the medulla and brain, the drug should not be administered either subcutaneously or intravenously. Too large a dose may lead to a fatal termination by causing paralysis of the respiratory center. According to Blake, the dose for children should probably never exceed one cubic centimeter for every twenty-five pounds of body weight. The dose for women should not be less, while the dose for a male adult probably should not be less than one cubic centimeter for every twenty pounds. The dose may be repeated from time to time according to the severity of the convulsions. In Blake's case the injections controlled the convulsions for periods varying from twenty-nine to thirty-seven hours each. It should be borne in mind, however, that the drug does not uniformly produce the same results, as will be seen in the report of one of Logan's cases, in which the injection produced no results whatsoever. According to Blake, magnesium sulphate is "reasonably safe and offers us a means of modifying the convulsions and relieving pain in a way no other drug has approached; for these reasons alone it is worthy of a more extended trial. It is not a specific treatment, but it produces anesthesia which may be taken advantage of for intraneural and other injections of tetanus antitoxin and for revising the site of infection."

Treatment.—Following this preliminary review of the so-called specific remedies we proceed to a systematic presentation of the treatment of tetanus. The latter may be said to be both prophylactic and active, local and constitutional. Sufficient has already been said of prophylaxis. At the first suspicion of tetanus the wound should be either eradicated or thoroughly disinfected, if this has not been done before, using as disinfectants remedies which may be said to be more or less chemical antidotes, carbolic acid and iodin. In order to prevent transpiration of the poison through the lymphatic system from the affected limb either Bier's passive hyperemia treatment may be resorted to or else a circular incision may be made around the limb down to the fascia. The necessity for prompt action in the treatment of tetanus will be appreciated when we realize, as has been aptly said, that when the symptoms appear the patient is not beginning to have tetanus, but is beginning to die from tetanus. Therefore in all cases in which the treatment is not begun until the first manifestations of the disease, we are badly handicapped, since the tetanus bacillus has had a start of some three to ten or more days before any measures are adopted to check its advance.

In the constitutional treatment there are three indications to be met: (1) to encourage free elimination and thus favor the withdrawal of toxin from already affected territories, (2) to protect hitherto unaffected territories, (3) to counteract the effect of the toxin upon cells already affected.

1. The first indication is met by encouraging free diuresis and diaphoresis. Since patients with tetanus perspire very freely, it is not necessary to prescribe diaphoretics, but the kidneys should be kept particularly active, as they are chiefly concerned in the elimination of the toxin. To this end water should be given freely to the patients, which is usually gratefully received because of their distressing thirst; but in addition to this, the action of the kidneys should be stimulated by the liberal use of saline solutions either intravenously or subcutaneously. For this purpose I should unhesitatingly recommend Matthews's salt solution (*vide* page 498), which not only allays irritation, but insures rapid elimination of the toxins.

2. In order to prevent the action of the toxin spreading to hitherto unaffected tissues we resort to the administration of one or two or more of the so-called antidotes—antitoxin, carbolic acid, or brain emulsion. The question will arise as to which of these remedies should be used, and whether one or more than one should be tried. Antitoxin should be used invariably unless unavailable; under these circumstances one must resort to Bacelli's or to the carbolic acid treatment. If the case is a very severe one, and did not respond promptly to antitoxin, one should not hesitate to resort to carbolic acid or brain emulsion (pp. 495 and 497), of course without interruption of the serum therapy. As to the method of administering the antitoxin: (1) 10 to 20 c.c. should be injected into the tissues about the wound; (2) 10 to 20 c.c. should be injected intravenously and into the muscles in order to neutralize the toxins circulating; (3) intraneural injections as near the cord as possible into the nerves of both upper and lower extremities (brachial plexus, sciatic and anterior crural nerves); (4) as suggested by Porter,[63] an immunizing or neutralizing injection may be given at the highest level which the severity of the symptoms appears to justify, directly into the cord as advocated by Rogers, or into the higher motor nerves, such as the hypoglossal and spinal accessory, as advocated by Porter; (5) if the injection directly into the spinal cord at a higher level is omitted, it might be well to carry

out Rogers's suggestion and inject the antitoxin *into*, not around, the nerves of the cauda equina.*

In the administration of antitoxin one should always be mindful of the fact that the serum is absolutely harmless and can be used repeatedly and in large quantities without any untoward effect. The doses, therefore, should be liberal and should be repeated daily or twice daily if necessary.

3. To counteract the effect of the toxins upon the cells already affected we resort to the use of certain physiologic antidotes—chloral, bromids, calabar bean, atropin, and morphin. Probably the best physiologic antidote is chloral; this may be given in 15-grain doses combined with the bromids. Calabar bean may be given in a dose of from $\frac{1}{4}$ to $\frac{1}{2}$ grain, 3 to 5 times a day. To control the pain and encourage sleep morphin is almost indispensable. It may be given to advantage with antimony $\frac{1}{8}$ to $\frac{1}{6}$ grain of each every two hours. A bottle of amyl nitrite should be kept in readiness and may be effectual in relieving those spasms of the glottis and the respiratory muscles which sometimes prove fatal. A drop or two should be applied to the nasal mucous membrane. In some cases it may be necessary to resort to a general anesthetic, preferably chloroform, particularly when the convulsions are unbearable or so frequent that the patient is rapidly becoming exhausted. In this class of cases one should not hesitate, if all other measures fail, to inject the magnesium sulphate solution or the morphin-eucain salt solution into the subarachnoid space.

It is needless to say that the patient should be isolated and kept in a room where he can be protected from disturbances of all kinds. A nutritious diet should be prescribed, preferably broths and milk, which it may be necessary to administer by a tube introduced either through the nares or through the mouth after the extraction of a tooth.

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* "In lumbar puncture it is necessary to wound one or more of the nerves in the cauda equina, as otherwise the injection is simply a subdural one which quickly passes from the lymph into the blood and can have no effect on the large charge of poison which is on its way up to the cord in the long nerves of the lower extremities. As the cauda equina begins opposite the first lumbar vertebra, a long needle should be inserted and manipulated back and forth until a twitching of one or both legs indicates that the desired nerve lesion has been produced. The injection of the antitoxin has then some prospect of being useful; from 10 to 20 c.c. are thus introduced in and around the wounded nerves. As this is manifestly working in the dark, I have often been tempted to perform a laminectomy in the lumbar region and to inject each nerve directly, as is done in the axilla or groin; but experience has not yet seemed to justify so drastic a procedure." [10]

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CHAPTER XIII.

DISEASES CAUSED BY SPECIAL INFECTIONS.

By Charles Harrison Frazier, M.D.,

PHILADELPHIA.

ANTHRAX.

Synonyms.—Charbon; Malignant pustule; Splenic fever; Woolsorter's disease; Milzbrand.

Definition.—A specific disease caused by the Bacillus anthracis, usually communicated from the domestic animals to man, and characterized by a pustular, edematous swelling and certain constitutional manifestations.

Historical.—Various outbreaks of plague affecting man and most species of animals have been described since the earliest historical times, many of which have been identified as anthrax. During the middle ages, particularly, a large number of epizoötics have been reported as occurring in Europe, some of which were anthrax while others were the related diseases of malignant edema, rinderpest, or black leg.

Chabert[1] (1780) classified and pointed out the symptoms peculiar to anthrax, but he and other writers of succeeding years attributed this disease to almost every condition to which animals might be exposed. Bad sanitation, ventilation, food, or forage; excessive atmospheric conditions, such as heat and moisture; or certain peculiarities in the soil, were all regarded by various authorities as etiologic factors. Heusinger[2] in 1850 declared anthrax to be a malarial neurosis dependent upon conditions of climate and soil. It was then observed that certain cases of malignant pustule in man could be directly traced to inoculation from animals affected with anthrax, and Barthélemy (1823) and Leuret (1824), and especially Eilert (1836), succeeded in producing the disease in horses and sheep by inoculation. Rayer and Davaine[3] (1850), Pollender[4] (1855), and Brauell[5] (1857) observed the presence in anthrax blood of rod-like bodies (*petits batonnets*), though they did not attribute to them the cause of the disease. Pasteur[6] in 1857 published his celebrated memoir on lactic acid fermentations, and this led Davaine[7] (1863) to believe that the bodies in anthrax blood were microörganisms. For some years a continual controversy was waged, until Koch[8] in 1877 succeeded in making cultures of the Bacillus anthracis and in reproducing the disease by inoculating animals with these cultures.

Etiology.—Anthrax is a contagious disease of the widest distribution. It is most commonly observed in various portions of Europe, particularly European Russia, Germany, Italy, and Great Britain; in

Asia, South Africa, and South America. It is not common in North America, North Africa, nor Australia. Statistics (from the "Jahresberichte über die Verbreitung von Thierseuchen") for the years 1901 to 1903 show that about 150,000 cases of anthrax in animals were reported in European Russia and the Caucasus, about 15,000 in Germany, and 12,000 in Italy. The transmission of the disease from animals to man is traceable in great measure to certain occupations and industries, chief among which are wool-sorting, wool-combing and spinning; hair-combing and brush-making; the hide and skin industry, mostly when the raw materials are handled; occasionally in various other occupations, particularly horn-workers, rag-sorters, butchers, farmers, and veterinaries. McFadyean[9] suggests that sporadic outbreaks in animals may be due to artificial manure and imported feeding-stuffs, especially those imported from Russia. Van mohair, mohair, alpaca, pelitan, cashmere, Persian, and camel's-hair are classed as the dangerous kinds of wool by Legge,[10] particularly those imported from Persia and Turkey. The source of infection from horsehair could be traced to that brought from China, Russia, Siberia, or South America. In hides and skins those imported from China, Bombay, and the East Indies were the most common carriers of infection. It is interesting in this connection to recall that Russell[11] in 1899 traced cases occurring in Wisconsin to hides received from South America and China, while Ravenel[12] in 1897 attributed 12 fatal cases in man and 60 in cattle to Chinese hides. That material imported from these countries is particularly liable to contain anthrax infection is due

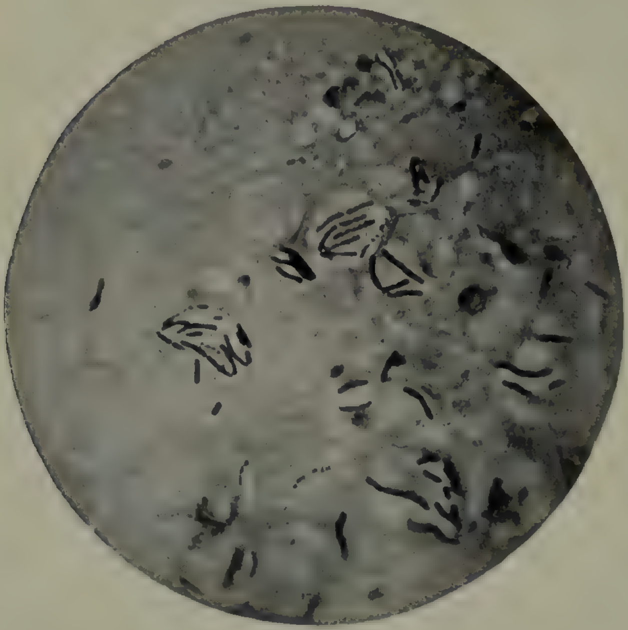


FIG. 134.—BACILLUS ANTHRACIS IN LYMPHATIC FLUID FROM FROG; PHAGOCYTES. × 500 (Fränkel and Pfeiffer).

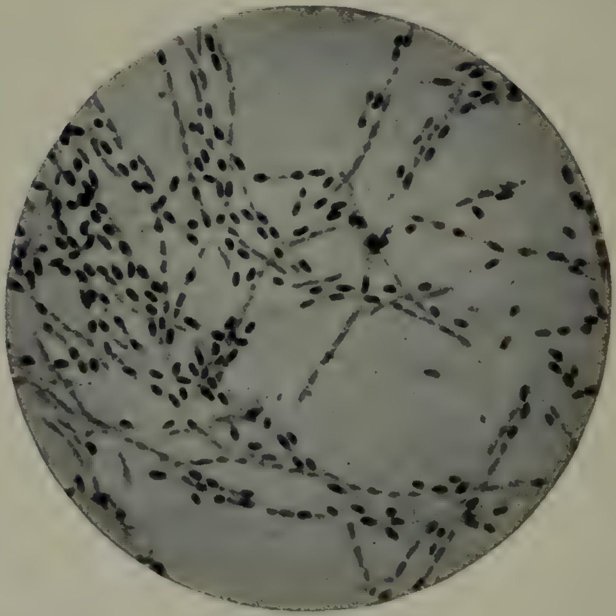


FIG. 135.—BACILLUS ANTHRACIS STAINED TO SHOW THE SPORES. × 1000 (Fränkel and Pfeiffer).

to climatic conditions. "Places liable to be flooded and drying out to a considerable degree in summer" (Billings[13]) characterize districts in Persia, Asia Minor, and the plateaus of Central Asia. A number of cases have been reported in Philadelphia, Pa., in the manufacturing districts of the city, such as Kensington and Manayunk, Willard[41] collecting 10 cases, with a mortality of 50 per cent. Finally, as in all infections, certain conditions of soil, moisture, temperature, and decomposing vegetable material play important parts. Thus months of July and August witness the most cases, and a moist soil, containing as it does so much putrefying organic matter, is believed to favor the growth of the organism. Males are affected far more commonly than females, 86 per cent. of the 261 cases collected by Legge[14] in Great Britain being males.

There are three portals of entry corresponding to the three clinical types of the disease, when the organisms are (1) deposited in wounds or abrasions of the skin, (2) are inspired, and (3) are ingested into the gastrointestinal tract. In Legge's cases only 6 were of the internal type, the remainder occurring in 85 per cent. upon the head, face, and neck. In 923 cases collected by Koch,[15] most of which were contracted from hides and skins, the head and face were affected in 48.4 per cent., and the upper extremity, particularly the fingers and hand, in 40 per cent. of cases.

Pathology.—Anthrax produces upon the external surface a somewhat elevated pustule, 5 mm. to several centimeters in diameter, with a depressed central scab. The corium and papillary body become infiltrated with a serocellular exudate and with bacilli. The perivascular and connective-tissue spaces become filled with leukocytes, and the pressure of this serous and cellular infiltrate, together with the toxins of the bacteria, cause the central coagulation necrosis, though suppuration does not occur unless there is a mixed infection. When the sero-cellular exudate extends upward to the superficial epithelium, it elevates the latter and produces the typical vesiculation. In the edematous variety the swelling is due to the diffuse sero-cellular infiltrate and to the effect of the bacteria blocking or inducing coagulation in the capillary vessels.

In the lungs the spores develop in the bronchi and alveoli, penetrate the walls, pass into the lymph spaces of the lungs and pleura, and thence into the bronchial and mediastinal lymph nodes. A gelatinous edema is produced in the tissues of the mediastinum, especially under the sternum and about the base of the heart, and there is a serous effusion, often hemorrhagic, in the pleural and pericardial sacs. Edema of the superficial tissues, especially of the neck and chest, and necrotic foci in the trachea or lungs have been observed.

In the intestinal form, in the small intestine particularly, the lesions consist of inflammatory hemorrhagic infiltration, with ulceration of the crests of the mucous folds, or of circumscribed hemorrhagic foci with a central slough surrounded by an edematous area. Occasionally the meninges are affected.

Symptomatology.—**Varieties.**—(1) Cutaneous anthrax—either the malignant pustule or edematous anthrax, the grave form of which is frequently styled erysipelatous anthrax. (2) Pulmonary anthrax—wool-sorter's disease. (3) Intestinal anthrax.

The Malignant Pustule.—Occurs most commonly upon the face, fingers, and hand. It is usually carried to the face by the fingers. The period of incubation varies from a few hours to several days. A small papule with a central bluish point is then observed, resembling an insect bite, accompanied by burning and itching. A few hours later the papule becomes vesiculated, contains a brownish, sanguineous fluid, and may be scratched off by the patient. The surrounding tissues become red, indurated, and puffy, and later purplish and gangrenous in appearance, although there may be no indication of suppuration. Pain now ceases, and beyond malaise, nausea, slight fever, and muscular or joint pains, there may be no other constitutional effect. A vesicular areola limited in extent is soon observed about the pustule, containing serohemorrhagic fluid; the pustule may undergo necrosis, the area of necrosis rarely exceeding 3 cm. in diameter. In about ten days, in favorable cases, a line of demarcation forms about the eschar, which "floats off," leaving a defect to heal by granulation. In more severe cases the edematous swelling about the pustule may be very extensive and erysipelatous in appearance, associated with a lymphangitis and lymphadenitis with hard and tender lymph nodes. The vesicles become bullæ, contain a bloody fluid, and the ultimate suppurative and gangrenous process may involve areas as large as the entire half of the face. In these severe cases the constitutional symptoms are marked, resembling those of cholera, with great prostration and depression, a weak rapid pulse, often icterus, diarrhea, delirium, and coma.

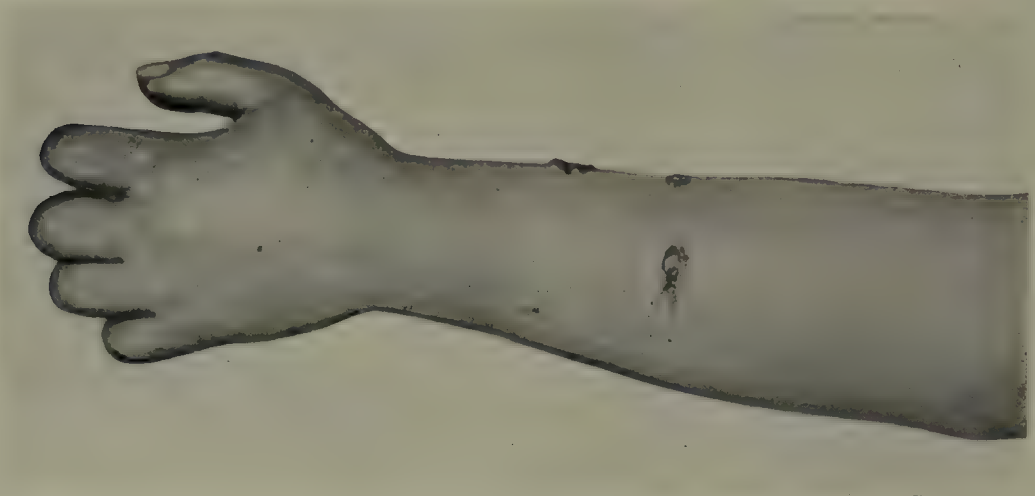
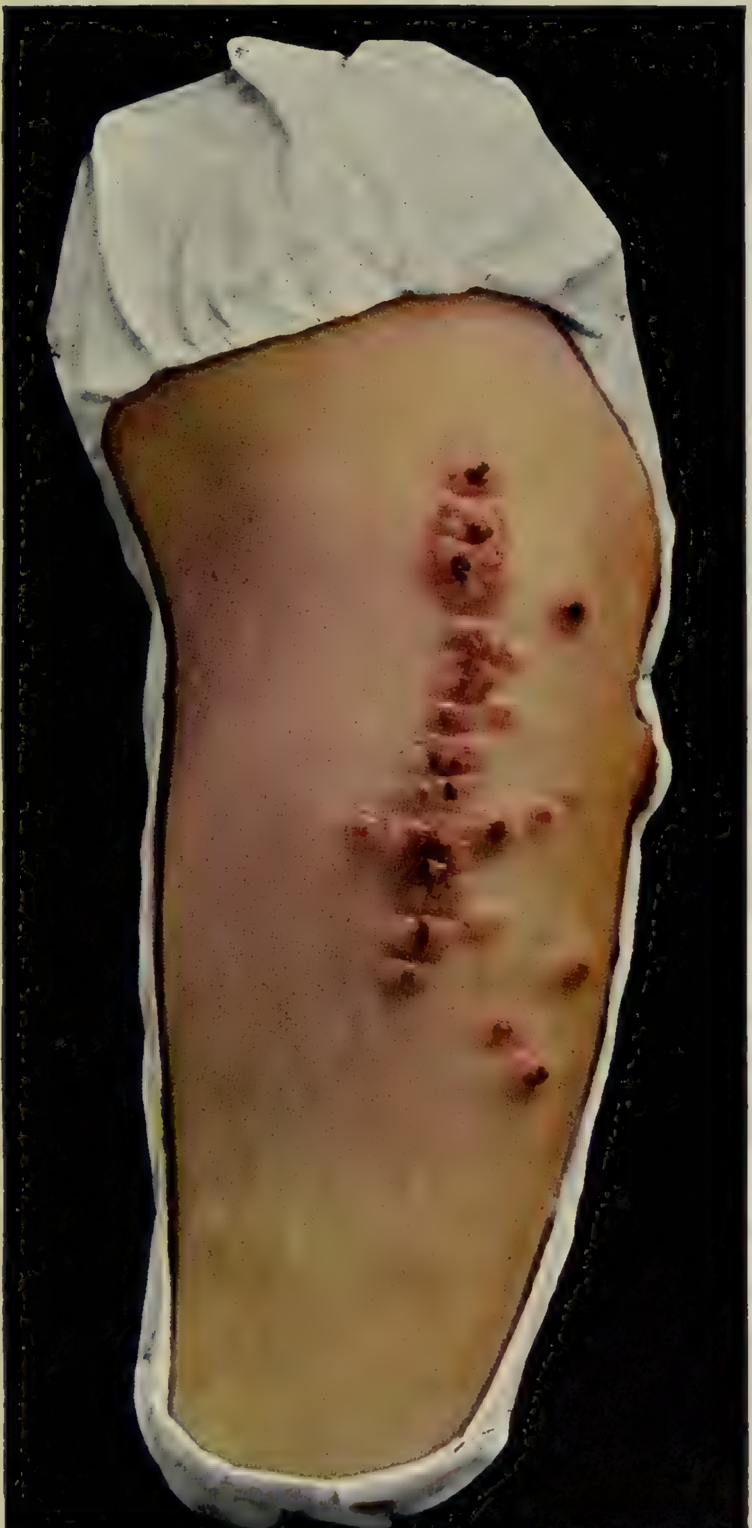


FIG. 136.—CASE OF ANTHRAX (Keen).

Edematous Anthrax.—This is most common in the loose areolar tissue, with scanty blood-supply, as in the tissue about the eyelids, neck, and forearm. Bourgeois[16] in 1834 and later in 1861 described this variety so thoroughly that but little has been added by subsequent writers. Bell[17] has observed seven cases. A diffuse flat edematous swelling occurs without well-defined borders and without the characteristic changes in

PLATE X.



Anthrax (Pustula Maligna) (Jacobi).

the skin, such as vesication or redness. There is no pain, fever, or eschar except in the most severe cases, and even in those resulting fatally the temperature is rarely high and there is little or no pain.

Pulmonary Anthrax.—"Wool-sorter's or rag-picker's disease" is most commonly observed in those working in dry, dusty wools, especially alpaca and mohair. Bell[17] and Eppinger[18] have described this form of anthrax exhaustively. It is not of surgical importance. Following slight premonitory symptoms, the patient is seized with a chill and complains of a feeling of tightness, weight, and oppression about the chest, with embarrassed respiration. A slight cough develops, rarely accompanied by expectoration. The face becomes dusky, the extremities cold and clammy, and the temperature rises to 102° or 103° F. The pulse is small, feeble, and irregular, and death occurs from collapse, sometimes preceded by convulsions and coma. The disease runs a short course, terminating fatally in 80 per cent. of cases before the fifth day.

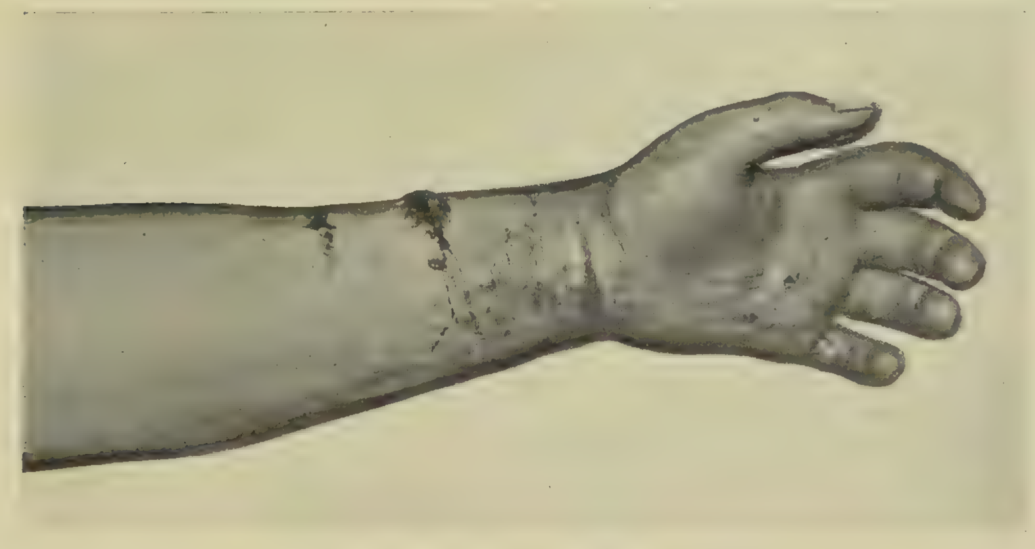


FIG. 137.—CASE OF ANTHRAX (Keen).

Intestinal Anthrax.—The symptoms which develop after an infection of the intestinal canal, after eating the flesh or drinking the milk of diseased animals, are like those of ptomain poisoning: general malaise, headache, chills, nausea, vomiting, and diarrhea. In addition to these, there may be hemorrhages from the mouth, nose, or rectum, frequently dyspnea and cyanosis, and, if the disease is not rapidly fatal, circumscribed areas of edema, hemorrhagic diarrhea, intense pain, and a small phlegmonous carbuncular eruption upon the skin. The latter is most frequently seen along the arm and about the head and is due to bacillary metastasis.

Diagnosis.—The occupation of the patient is most significant. The malignant pustule must be distinguished from furuncle and carbuncle. The furuncle is conical, contains the central slough, does not have the edematous areola or the vesiculation. A carbuncle is a furuncle with multiple openings, is exceedingly painful, suppurates freely, and does not vesiculate. In doubtful cases animal inoculation will decide the diagnosis in two days, or a cover-slip preparation may immediately demonstrate the anthrax bacillus, which is readily stained. Sheen[26] has reported a case where the accidental inoculation of the cheek of a woman by a recently vaccinated child simulated cutaneous anthrax.

Edematous anthrax may resemble erysipelas, but the abrupt line of demarcation, the high fever, the circulatory disturbances, and the early and profound prostration should serve to differentiate the two. Acute emphysematous gangrene (malignant edema, etc.) is characterized by the history of an injury, severe pain, hyperpyrexia, rapidly spreading gangrene, and emphysema terminating fatally after within twenty-four to forty-eight hours. Peterson,[19] however, has reported a case of compound fracture of the leg of a man, necessitating amputation later, whose duties required him to mix animal's hair with lime in making plaster. Cultures from the wound discharged revealed a large number of anthrax bacilli. Microscopic examinations should always be made of the wound secretions, the blood, or the feces, for the purpose of determining whether the offending organism is the anthrax bacillus or the bacillus of malignant edema, the bacillus aërogenes capsulatus. In Keen's case[42] the diagnosis was easily and quickly established by a stained cover-slip smear from the blood.

Prognosis.—Anthrax is a very fatal disease. Koch[20] collected 1473 published cases of malignant pustule with a mortality of 32 per cent. In Italy, Sclavo[21] collected 24,052 cases (1880–1890), with 24 per cent. mortality. In St. Denis and the Department of the Seine[22] 123 cases (1886–1893) gave a mortality of 28.4 per cent. In England (1899–1904) Legge[23] collected 261 cases, with 25.6 per cent. mortality. The mortality is highest when the lesion is situated upon the head and face, particularly the upper lid and eyebrow, and lowest where the extremities, particularly the lower, are involved. The possibility of applying stronger bactericidal agents to the extremities than to the face accounts for this difference in the mortality. Senn[27] says that "as a general rule, it may be stated that the firmer and more circumscribed the local lesion, the more favorable the prognosis, and, vice versa, the more extensive the area of infectionand the more diffuse the edema, the greater the danger to life from general infection." Pulmonary and intestinal anthrax are very fatal, though of late years the mortality has been decreased by the use of an antitoxin. Following Pasteur's test inoculations at Pouilly-le-Fort in 1881, vaccination of animals has been extensively practised in France, and later in Italy, with excellent results. According to Chamberland,[24] the mortality has been reduced in sheep from 10 per cent. to 1 per cent., and in cattle from 5 per cent. to ½ per cent. According to Sclavo's statistics,[25] of 164 cases of human anthrax in Italy treated by serum inoculations, the mortality was 6.09 per cent.

Treatment.—As the greater number of cases of anthrax are of the external or cutaneous variety, the treatment in the past has consisted in the application of certain medicated substances or in excision of the pustule. A glance at the mortality shows how ineffective these measures are. The efficacy of excision depends to a great extent upon the duration of the infection. When performed early, it will be followed in many cases by a subsidence of the edema and a fall in temperature, but the mechanical injury done to the tissues by the knife, the opening of new paths of infection through the lymph sinuses and blood-vessels, and the resulting scarring and disfigurement, particularly about the face, must be regarded as objectionable features of this plan of treatment. If any operation is done in a case of anthrax, it should not be done in the ordinary operating room, but in a separate room. After the operation, the floor should be thoroughly disinfected and a bacteriologic examination of the floor made in order to determine whether the disinfection has been effective. In Keen's case at the Jefferson Medical College Hospital, three disinfections by formaldehyde, pure carbolic acid, and strong bichlorid of mercury were required before the floor was found to be germ-free.

Rigidly conservative measures have been advocated by many writers, particularly K. Müller,[28] Ramstedt,[29] and more recently Strubell[30] and Schultze.[31] Müller treated 13 cases and Ramstedt 7 cases by rest, fixation, and the local application of mercurial ointment; Strubel recommends the application of hot cataplasms supplemented by injections of a solution of carbolic acid; and Schultze applies hot compresses of a 1 per cent. mercuric chlorid solution in 70 per cent. alcohol.

Injections of carbolic acid solutions are frequently employed, particularly in Russia, and Scharnowski[32] claims to have treated 50 cases with only 2 per cent. of deaths by this method. Sassi[33] injects 5 drops of pure carbolic acid into three parts of the carbuncle (15 drops in all) and repeats the dose if necessary. Graef[34] collected 384 cases treated by caustic potash with a mortality of 5 per cent. These figures show the fallacy of generalizing upon a few cases when larger groups of cases give a so much greater death-rate. In keeping with the progress of serum therapy in other diseases, an immunizing agent has been developed, which promises to be as effectual in the treatment of anthrax as the antitoxin has been in the treatment of diphtheria. Touissant[35] in 1880, Pasteur in 1881, Marchoux[36] in 1895, and Sobernheim[37] in 1898 and later in 1902 and 1904, have contributed important articles to the subject of immunity to anthrax based upon experimental work. Pasteur and Chamberland in France and Sobernheim in various portions of Europe and South America have treated thousands of sheep, horses, and cattle with inoculations of serum. Sclavo[38] in June, 1897, began the treatment of anthrax in man by a serum prepared by the combined active and passive immunizing treatment (simultaneous inoculations of serum and virus) of animals, particularly the ass, from which the most powerful serum is obtained. In 1903 he collected 164 cases which had been treated by the serum with a mortality of 6.09 per cent. Legge in 1905 collected 67 published cases with 2 deaths, a mortality of 3 per cent. A number of additional cases have been reported by British writers [39] with two deaths.

It is claimed for the serum treatment, that it is innocuous in large doses, even when introduced into the veins; that it is of particular value in the early stages or in cases of moderate severity, and at the same time of great benefit to cases of the graver form. The possibility of suffocation from extensive edema and the tendency to tissue destruction are reduced to a minimum.

In such situations as the eyelid, where local treatment is out of the question, and in internal anthrax the serum treatment holds out the only hope of success. The dose, as advised by Sclavo, is 30 to 40 c.c., subdivided into three or four parts, injected at different points into the abdominal wall. The dose may be repeated in twenty-four hours if no improvement has occurred. In grave cases 10 c.c. should be injected into one of the superficial veins upon the back of the hand, and the dose repeated if necessary in an hour or two. Bandi[40] believes that larger doses should be used (as much as 150 c.c. at one time) "in cases of anthrax in man which show a decided tendency to generalization, and especially in such as are marked by the phenomenon of poisoning (diffuse edema, disturbances of the circulation, renal lesions, etc.)." In such cases Bandi thinks that Sclavo's method, which is designed to induce a reaction upon the part of the organism, fails because of the virulence of the poison, and that an attempt should be made, therefore, to neutralize the circulating toxins as completely and rapidly as possible. Since in such large doses the ether which is used as a preservative might be harmful, Bandi recommends that the serum, while still hot, be poured into a sterilized glass vessel covered with sterile gauze. By this procedure the precipitate being filtered out most of the ether will evaporate.

Judging from the experience of those who are most qualified to speak, the treatment of anthrax should consist essentially in the administration of Sclavo's serum, in the excision of the pustule, and in the application of certain bactericidal agents. The serum should be administered subcutaneously and the pustule should be excised only when the surrounding tissues are not very edematous, taking the precaution to cauterize the exposed surfaces with carbolic acid or the actual cautery. If the edema is marked, absolute rest of the part should be enjoined and local hot antiseptic fomentations, such as carbolic acid or bichlorid of mercury, applied. The serum has no deleterious effects, and in the hands of its originator and others, especially in Italy and England, the results substantiate the claims which have been made. It assists in the destruction of the bacilli, before they become so numerous that their destruction by the bodily defences increases the danger of fatal poisoning from the toxins set free by the disintegration of the bacilli.* When the serum cannot be obtained, and when excision is impracticable, injections of carbolic acid (5 per cent.) should be tried, introducing the needle at several points along the margin of the pustule and infiltrating the base of the pustule and surrounding healthy tissue. These injections may be repeated frequently. The constitutional symptoms must be met by appropriate stimulants and supportive measures.

Prophylaxis.—If it were possible, sheep from countries where anthrax is prevalent should be washed previous to shearing, the wool willowed from dirt, and the fallen fleeces discarded or classed apart. In England "none of the dangerous specified wools (alpaca, pelitan, cashmere, Persian, camelhair, and mohair) may be opened or sorted except at a place where a constant draught of air maintained by a fan carries the dust away downward" (Legge). Respirators should be worn especially in places where no such down-draught is provided. Rubber gloves also would be a protection to those handling possibly infectious material, except in cases in which the sense of touch must not be lessened by such gloves. It is possible that disinfection by steam, not only of wool but of horsehair, may be made possible by improved apparatus in the future. In Germany and in England experiments have been carried on with this intent. More frequently the disease is transmitted from hides and skins, and therefore to men employed on the wharves, docks, warehouses, and tan yards, and particularly from hides imported from China. Unfortunately but little can be done in the way of prevention except to impress upon those handling the skins the importance of general cleanliness. Russell[11] finds that when the hides were immersed in a solution sufficiently strong to kill the spores, the formaldehyde damaged the material. It is needless to say that the bodies of all infected animals should be burned.

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* Sclavo's serum can be obtained from the Bureau of Health in Philadelphia.

The factory and workshop rules for Great Britain class trades dealing in wools as dangerous and prescribe that those employed in wool-sorting, combing, etc., must wear suitable overalls while at work, wash the hands before partaking of food, which must not be eaten in the workroom, and must not work with any open sore or cut. Respirators are required to be worn by persons engaged in collecting and removing the dust from the floors.

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GLANDERS.

Synonyms.—Malleus humidus; Farcy; Morve; Rotz.

Definition.—A specific, infectious disease, common to horses and certain other animals, transmissible to man, caused by the Bacillus mallei, and characterized by the presence of multiple inflammatory foci, especially of the lungs, nasal passages, skin, and subcutaneous tissue.

Historical.—Glanders was known to the Greek and Latin writers, as occurring in horses and asses, and was described under the name of "malleus" in the fourth century by Apsyrtus (Hecker).[1] Even in 1749 the elder Lafosse,[2] of Paris, denied the contagious nature of the disease, the latter view having been previously expressed by Rufus, Ruini, and Winter, and taught that it was a local disease of spontaneous origin. This doctrine, which had many adherents, precipitated a remarkable controversy, especially in France, and was responsible for a great outbreak of glanders in the continental countries. In 1821 Schilling,[3] in Germany, and in 1837 Rayer,[4] in France, recognized the occurrence of glanders in man. In 1841 and 1842 a series of animal inoculations established the contagious nature of glanders, and Saint-Cyr[5] in 1863 proved that the chronic as well as the acute form was contagious. In 1882 Löffler and Schütz[6] in Germany discovered the Bacillus mallei. In 1891 Korányi[7] demonstrated the value of mallein as a diagnostic agent, a substance first prepared by Helmen.

Etiology.—Glanders occurs in man, horses, asses, mules, field-mice, cats, guinea-pigs, squirrels, rabbits, goats, and the dove. Carnivorous animals are said to become infected by eating meat infected with glanders. In man the disease is almost entirely confined to those whose occupation brings them in contact with horses. Thus, stablemen, coachmen, farmers, horsedealers, cavalrymen, veterinary surgeons, etc., are the ones most frequently attacked. Women may contract the disease, especially when employed in stables or belonging to a family of an individual employed about horses. Direct transmission from man to man has occurred only twice, according to Councilman.[8] The disease is contracted from the secretions of the infected horse, through a wound of the skin or by way of the respiratory or gastro-intestinal tract. Glanders appears in both horses and man in its acute and chronic form; the pathologic lesions are practically the same in man as in the horse, although there is considerable variation in the clinical manifestations of the disease in the two. While in most text-books the clinical phenomena as they appear in the horse are elaborated upon in great detail, it may be said that they are of little or no practical significance in so far as concerns the diagnosis of glanders in man.

Pathology.—The glanders bacillus produces a lesion characterized by necrosis, exudation, and proliferation of tissue, similar in many respects to that of the tubercle bacillus. The infection is usually pure, although mixed infection may occur. The original site of infection, if on the skin, frequently exhibits an intense inflammatory reaction, but through the medium of the circulation the infection is rapidly disseminated to other organs and tissues, particularly the lungs, muscles, and skin.

The Pulmonary Lesion.—In acute cases the lung becomes congested, frequently edematous, and the bronchi contain a thick, mucopurulent secretion. Numerous pneumonic foci will be found, most of them terminating in abscess-formation, but rarely appearing as nodules, varying in size from a pin's head to a walnut. It attained the latter size in a case recently reported by Post.[9] The pneumonic areas consist of a central exudate, composed of leukocytes, nuclear débris, and red cells, surrounded by a zone of hemorrhage, leukocytes, and fibrin. Giant cells and epithelioid cells have been observed. The abscesses are formed by the liquefaction of this exudate. Foci may be found beneath the pleuræ, and these usually become adherent to the lung.

The cutaneous lesions resemble those of the pyogenic infections and affect both the skin and subcutaneous tissues. The inflammatory exudate is composed of leukocytes, mononuclear and polynuclear, and the affected tissue often undergoes necrosis. Thrombi form in the blood-vessels, surrounding these foci. The epidermis may be separated from the necrotic focus by a fluid exudate, which may in turn separate the individual epithelial cells or dilate the lymph sinuses about the pustule. According to Councilman, "the lesions in the mucous membranes are similar to those in the skin with the exception that there is a great deal more extensive proliferation of the fixed cells." The intramuscular abscesses, resembling those in the lung and skin, present a central necrotic area surrounded by a thin wall of hemorrhagic and edematous tissue. Sometimes this cellular exudation surrounding the abscess is not present and the line of demarcation between the abscess and surrounding muscular tissue is sharply defined. Abscesses may develop in the testicles, bone-marrow, and liver, and in several cases the meninges were involved.

Symptomatology.—**Acute Glanders.**—A few days after exposure to infection, the source of which is sometimes obscure, the patient suffers from malaise, general weakness, slight chilliness, and pain in the limbs. There is fever, sometimes diarrhea, and many of the reported cases were at first mistaken for typhoid fever. In other cases sharp pains in the side of the chest, a few râles, and areas of dullness suggest a pleuropneumonia. The temperature continues to rise and may reach 103° or 104° F., with marked diurnal variations, associated with rigors. The headache, usually frontal in location, suggests an infection of the frontal sinuses from the air-passages. In ten days to two weeks hard swellings appear in the subcutaneous tissues and muscles, most commonly in the biceps, flexors of the forearm, the rectus, and the pectoral muscles. These are hard, movable, do not at first involve the overlying skin, but later become soft and fluctuating; the overlying skin breaks down and a mucoid, sanious fluid is spontaneously discharged. Sometimes a pustular eruption appears on the skin, especially of the face, and about the joints, resembling in some respects smallpox, but not umbilicated. This eruption, as a rule, appears late in the course of the disease, but may be noted as early as the second week. The joints, particularly the knee, become swollen and painful, and the synovial fluid if aspirated will be turbid and may contain the bacillus mallei. Those cases in which the articular symptoms are a conspicuous feature have frequently been mistaken for articular rheumatism. The nasal discharge is not as noticeable in man as in the horse, although the mucous membrane is usually swollen and injected with a fetid secretion. Ulcers and occasionally nodules have been observed in the mucous membranes of the nose and larynx. Since the lungs are almost invariably involved, a careful physical examination should always be made, and will usually detect the presence of a few râles or the physical signs of a bronchopneumonia. During the second or third week the patient becomes delirious, the temperature remains high, with marked diurnal variations, the skin dry, the mouth foul, and epistaxis is frequent. As the case progresses the physical signs in the chest are more rapidly detected, and, finally, about three weeks from the onset of the disease the patient dies.

Chronic glanders may last months or even years, in some cases terminating in recovery; in others, after a sudden exacerbation of the symptoms resulting in death. The hard nodules which appear in the subcutaneous tissues and muscles eventually break down, discharging a bloody purulent fluid, and appearing as obstinate, chronic ulcers, which resemble broken-down gummata. These lesions may be situated in the extremities, the face, the nose, the hard palate, and elsewhere. In fact, the multiplicity and wide distribution of the lesions is rather characteristic, although in several cases the nodules were confined to one extremity.

Diagnosis.—In the early stages of the acute variety a correct diagnosis is difficult, and, in fact, as shown by the reported cases, is rarely made. With the appearance of the pustules and the nodular swellings in the muscles and subcutaneous tissue the diagnosis may be established, if upon examination the Bacillus mallei is found in the fluid contents of these lesions. The occupation of the patient is of great significance, since the disease affects almost invariably those handling horses. The pustular eruption might resemble smallpox, but it is not umbilicated, and the individual lesions vary greatly in size and are frequently surrounded by a limited area of bullæ filled with a hemorrhagic exudate.

Anthrax is characterized by the presence of a central eschar, by the wide distribution of the vesicular or bulbous eruption, and by the absence of subcutaneous nodules. The phagedenic ulceration leaves behind large sloughing areas with an offensive discharge. The greater variability of the temperature, the frequent slight chills, the presence of a leukocytosis, and a negative Widal reaction in glanders will easily differentiate this affection from typhoid fever. Sweats, acid urine, a history of exposure to cold and damp, the involvement of successive joints, and the subsidence of the process in the joints first affected would point to rheumatism. In pneumonia an initial chill, high temperature, immediate prostration, are more characteristic of pneumonia, although physical signs in the lungs of glanders patients may be very confusing. The appearance of the characteristic pustules and nodules, it would seem, should suffice to confirm the diagnosis, although even under these circumstances the cutaneous lesions have been regarded as a furunculosis secondary to septic foci in the lungs. In 1889 Strauss[11] recommended the inoculation test for diagnostic purposes. He injected some of the exudate, containing the bacilli, into the abdominal cavities of male guinea-pigs and found in two or three days peculiar suppurative lesions of the peritoneum. Unfortunately these lesions may occur after the injection of certain non-pathogenic microörganisms. The serum reaction has been so little used on man that its value as a diagnostic agent is unknown. Heanley[10] investigated the reaction in two cases of glanders in which the diagnosis was verified by guinea-pig inoculations; in both cases the results were negative, although the sedimentation test gave a positive reaction.

Prognosis.—The prognosis should always be guarded; the acute variety is almost always fatal, though the chronic may persist for months. About one-half of the chronic cases ultimately recover.

Treatment.—The treatment may be said to be both local and constitutional, but of these the local treatment is by far the more important. Stimulant and supportive remedies should be used liberally, and iodin, arsenic, or creosote may be used internally. The point of inoculation, if discoverable, should be thoroughly disinfected, the nodules and abscesses should be opened with the thermocautery, disinfected with carbolic acid or chlorid of zinc in solutions (15 per cent.), and covered with antiseptic compresses. The primary nodule should be excised. Mercurial ointment has been used with some cases, and in one case of the chronic type (Bonome[12]) the patient's recovery was attributed to the use of mallein. In animals the disease can be readily detected by the mallein test. All diseased animals should be killed and their carcasses burned and the stables disinfected. It is worthy of note that the most virulent cases develop in animals with improper hygienic surroundings, such as poorly ventilated and badly lighted stables.

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ACTINOMYCOSIS.

Definition.—A specific infectious disease common to many of the domestic animals and occasionally occurring in man, caused by a specific microörganism, the *actinomyces bovis*, and characterized by destructive inflammatory lesions and the formation of extensive granulation tumors.

Historical.—Langenbeck[1] in 1845 recognized the presence of the sulphur-grain-like bodies in the pus of a case of vertebral caries. Lebert[2] in 1857 published a description of fungi found in a thoracic abscess observed by Louis in 1848, and believed them to be the débris of *cysticerci*. Rivolta[3] (1868), Perroncito[4] (1875), and Bollinger and Harz[5] (1876), studied the "lumpy jaw" of cattle, and the latter writers recognized the characteristic fungus and termed it actinomyces. Israel[6] in 1878 observed the occurrence of this parasite in man, and Ponfick[7] (1879) identified the granules found in the "lumpy jaw" of cattle as those of actinomycosis hominis. A large number of articles, mostly controversial, then appeared in Germany and Italy, and the disease was studied with great care from both its clinical and pathologic aspects. Johne[8] was the first to perform inoculation experiments, and succeeded in reproducing the disease from the fungus. In England the first case in man was observed by Acland in 1884, and in this country Murphy reported the first case in 1885.

Biology and Morphology.—The actinomyces hominis has recently assumed greater pathologic importance than was formerly accorded it, owing to the increasing number of recognized cases of infection in this country as well as abroad. It lies between the bacteria and moulds, some investigators classing it with the former and others with the latter.

There are many varieties, both pathogenic and non-pathogenic, and apparently considerable variation in the individual forms, so that confusion in classification has arisen. In cultures—best obtained on dextrose agar at the temperature of the body—it grows in long thin threads (mycelium) with many branches. Vacuoles and granules are frequently seen when stained (carbol-fuchsin, Weigert, Gram). It is essentially an anaërobe. It is so tenacious of life that successful inoculations have been made from dried material preserved as long as nine months. A temperature of from 60° to 85° C. is fatal in from three to five minutes. Toxins probably exist, but little is known concerning them.

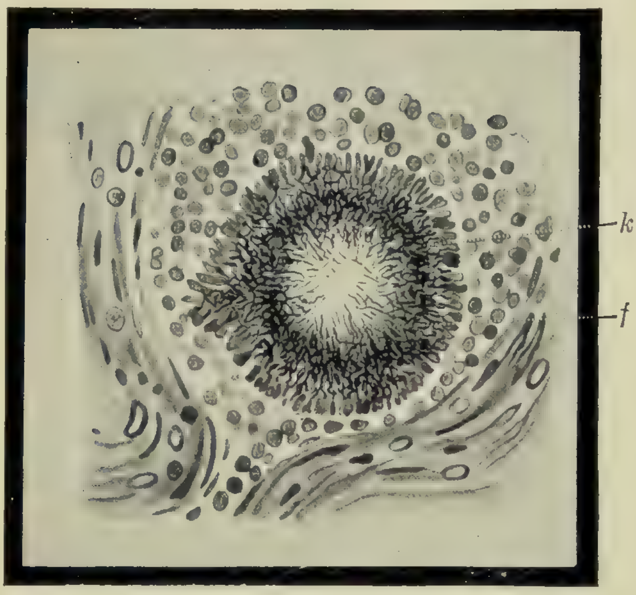


FIG. 138.—ACTINOMYCES.
Section from human being. *k*, Club-shaped bodies; *f*, thread of mycelium; × 800 (Marwedel).

In animal tissues the ray fungus usually grows in a characteristic manner, forming colonies the size of grains of sand scattered throughout granulomata of considerable size, perhaps floating in accumulations of pus. This arrangement, however, does not always exist, the organism often occurring singly instead of in colonies. These "sulphur-grain" bodies or *drüsen* vary from 0.5 to 1.0 mm. in size, their color being translucent gray, yellow, red, or even green or black. They are easily visible to the naked eye, especially in pus. In young colonies they are soft, but in the older ones they are quite firm, even to the point of grittiness from the deposit of calcareous salts.

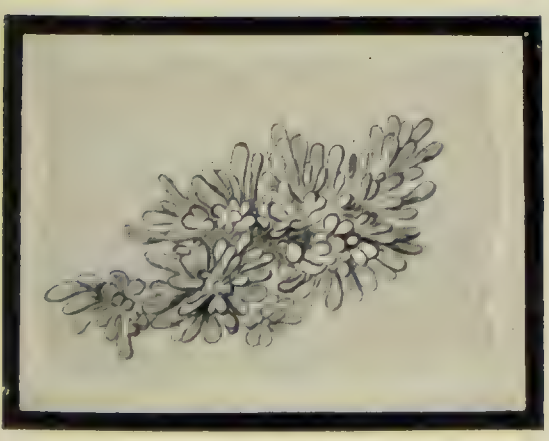


FIG. 139.—GRAINS OF ACTINOMYCES FROM HUMAN PUS; × 450 (Marwedel).

The granules represent single colonies or groups of colonies. In their center is a mass of tangled mycelium inclosing numerous round bodies like cocci (spores?). Toward the periphery of the colonies the threads tend to place themselves in a radiating manner, their ends being often distinctly clubbed. But this definite wheel-like arrangement is often interfered with by irregular projections of branching mycelium, and the clubs may be altogether absent. Even the threads are so broken up at times that they can be found with difficulty only, thus giving rise to much uncertainty in the microscopic, if not in the clinical diagnosis.

In examination with the microscope, it is seldom necessary to employ differentiating stains, the inspection of a granule which has been washed in sterile water flattened beneath a cover-glass being usually satisfactory.

Etiology.—Actinomycosis is of wide distribution, having been observed throughout Europe, in Australia, Egypt, Algeria, and on various islands. About 125 cases have been reported in the United States. The disease is one of young adult life, particularly of the third and fourth decades, and about 70 per cent. of cases are in males. Race, season, climate, occupation, or social condition do not appear to be influential factors. As is usual with most infectious diseases, unfavorable hygienic conditions and surroundings act as predisposing causes.

Methods of Infection.—**From Cattle.**—There is no definite evidence to support the theory that the disease may be transmitted from cattle. The patients reported to have suffered from the disease are engaged in such a variety of pursuits that occupation cannot be used as an argument in favor of the transmissibility of the disease from animal to man, in fact, but few cases have been observed in which such transmission is believed to have occurred. There is practically no danger from consuming the flesh of animals affected with actinomycosis, though the using for food of infected carcasses is forbidden in this country.

From Cereals.—Jensen [13] in 1880 observed that actinomycosis was prevalent in cattle which had been fed on barley grown on land reclaimed from the sea, and Johne[14] (1881), Bostroem[15] (1885), Piana[16] (1885), Brazzola [17] (1888), and Hofmann [18] recorded the occurrence of actinomycosis in vegetable substances embedded in the tonsils, tongue, or pharynx of cattle, Hofmann's observation being on a case in man. Following these observations numerous other cases have been reported where either portions of grain have been found in the actinomycotic lesion or patients were in the habit of chewing raw grain or carrying strips of straw in the mouth, as in Poncet's [19] case. Hudson [20] in this country observed a case in which the lesion was attributed to a piece of oat straw which stuck in the patient's tongue and could not be disengaged. Leith [21] has reported a case where the patient was in the habit of chewing grain. Bostroem,[22] in a later article, devoted chiefly to the biology of the actinomyces, commented upon its frequent association with grains; other investigators, particularly Gasperini,[24] have shown that this and similar organisms are widely distributed in cereals, grasses, etc. The question, however, has been considerably complicated recently by the appearance of Wright's [23] study of the microörganisms of actinomycosis; he takes exception to the work of Bostroem and Gasperini and concludes that the organisms with which they worked were *Nocardia*. The actinomyces bovis is, he believes, a normal inhabitant of the secretions of the buccal cavity and of the gastro-intestinal tract of both men and animals. In regard to the mode of infection, Wright says, "that the part played by foreign bodies so frequently found in actinomycotic lesions is not that of the carrier of the microörganisms into the tissues from without, but that the foreign body, by its traumatic and irritative effect, furnishes a nidus in the tissues for actinomyces, which enters therein with the secretions from the buccal cavity and gastro-intestinal tract, develops into characteristic colonies, and produces lesions which we call actinomycosis."

Site.—Ruhräh [25] tabulates 628 cases from different observers with the following result: head and neck, 359—55 per cent.; digestive tract, 132—19 per cent.; pulmonary, 92—14 per cent.; skin, 16—2 per cent.; doubtful, 33—5 per cent. Hichens in 1905 collected all the cases reported in the British Islands, with the following results: head and neck, 27—34.17 per cent.; abdomen, 39—49.3 per cent.; thorax and lungs, 12—15.18 per cent. Stanton [38] recently has reported a case of actinomycosis in which the disease was limited to the urinary tract, a very unusual site.

Pathology.—The lodgment of the ray-fungus in the tissues is followed by an inflammatory reaction, progressive in character, characterized by a cellular infiltration, necrosis, and the formation at first of granulation tissue and later of fully organized connective tissue. According to Firket,[9] the cellular hyperplasia, not coagulation necrosis, is the first phenomenon. The fungus develops a mycelium and a fungus-granule and is soon surrounded by an area of small round cells, and later of corpuscles, giant and epithelioid cells. In the neighborhood of the cellular exudate the connective-tissue element proliferates, forming embryonic granulation tissue with new vessels. The gradual extension of the process, by the transportation of mycelial filaments, either by the phagocytes or along the lymph channels, with the attendant cellular infiltrate and granulation tissue formation, may result in the formation of tumor masses resembling neoplasms, especially the sarcomata. This neoplastic form, though occasionally seen in man, is the one usually found in horses and cattle and gives rise to the so-called "lumpy jaw." The tumor contains, in addition to the cellular mass, numerous foci of disintegration, in which the characteristic granules are observed. In man the lesion is more inflammatory in its manifestations; suppuration is a frequent complication, since tissue-necrosis is a more conspicuous feature than tissue-proliferation. The disease travels along the connective-tissue planes, producing branching sinuous tracts and fistulæ, lined by granulation tissue upon a hyperplastic connective-tissue base and containing the typical granules. Suppuration is due to a secondary infection, since the actinomyces itself is not a pyogenic organism. This is more readily understood as the portals of infection are recalled, viz., the mouth, the gastro-intestinal or respiratory tracts, and the cutaneous surface. According to Wright,[10] the progressive character of the disease might be attributed in some cases to the ever present source of infection in the buccal cavity and in the gastro-intestinal tract, admitting his assumption that the actinomyces bovis is a regular inhabitant of these cavities. Of all the bones, the inferior maxillary is the most commonly involved. According to Baracz,[11] the bones are never, as Poncet would have us believe, the seat of a primary lesion. The process is usually a destructive one and is attended with active proliferation from the periosteum and the formation of a new shell of bone, which adds to the size of the tumor. Primary actinomycosis of the intestinal tract manifests itself as a superficial invasion of the mucous membrane in the formation of whitish patches (Chiari[12]), or in the more diffuse variety by the formation of nodules beneath the mucosa. These nodules undergo degeneration, ulcerate, and, rapidly extending beyond the original site, invade the peritoneum, retroperitoneal connective tissue, and various organs, especially the liver. The retroperitoneal infection may travel downward into the pelvis, invading especially the perirectal tissues, or upward, through the diaphragm into the pleural cavity. As a result of the peritoneal invasion numerous adhesions form which, while preventing a general peritonitis, at the same time might seriously embarrass the surgeon in an attempt to eradicate the disease. Direct communication may be established at the site of an adhesion between one loop of intestine and another, between the intestines and bladder, and between the intestine and the external surface of the body through fistulous tracts in the abdominal wall. Pulmonary actinomycosis is characterized by the development of a bronchopneumonia about the focus of infection, by the dissemination of the fungus and the formation of nodules in the lung, surrounded by new granulation tissue; the contraction attending the organization of the granulation tissue may convert the lung into a functionless connective-tissue mass. In most cases the nodules undergo softening, and by the destruction of lung tissue, and by secondary infection, abscess cavities form, which contain pus, fatty detritis and fat crystals, blood, and masses of actinomyces. The pleuræ, the pericardium, and mediastinum soon become involved. *Metastasis* occurs, principally by continuity or, as in the abdomen, by contiguity. Rupture may occur into the blood-vessels, usually the vein, and the infection be carried to distant localities, such as the skin, bones, muscles, brain, kidneys, or by way of the portal vein into the liver. The portal of entry in some of the cases is hard to determine. This is particularly true of primary lesion of the brain or liver. *Regional dissemination never occurs through the lymphatic channels*, and if the nodes are enlarged it is an indication rather of secondary infection.

Symptomatology.—The clinical manifestations of actinomycosis may most conveniently be studied under the following groups: (1) Cervico-facial, (2) thoracic, (3) abdominal, (4) cutaneous actinomycosis.

1. **Cervico-facial Actinomycosis.**—In this, the most frequent locality, the fungus enters the tissues by way of minute abrasions in the mucous membrane of the buccal cavity, or through the softened and swollen gums about decayed teeth, and usually invades the jaw and adjacent tissues. The symptoms are pain, the early appearance of rigidity of the muscles concerned in mastication, and the slow formation of an inflammatory, indurated, almost boggy swelling, without enlargement of the lymph nodes. The pain, though not always present, is like the pain of a toothache, and is due to the pressure of the associated inflammatory reaction. Tenderness is not often observed. Trismus is rarely absent and is caused

by the infiltration of the muscles of mastication. When the cheek is invaded the masseter and, in extensive infections, the pterygoid and temporal muscles may be so involved as to affect articulation and prevent the patient opening the mouth but a short distance. The swelling, together with the trismus, is the most constant symptom, and when sharply circumscribed may resemble a sarcoma. In the majority of cases the swelling appears first at the angle of the jaw, increases in size very slowly, is circumscribed and infiltrating. It is hard, dense, and nodular, penetrates the cheek in front of the masseter muscle, and extends to the surrounding tissue. The skin soon becomes of a bluish-red color and areas of softening may be felt, fluctuating or boggy, which soon ulcerate and discharge their contents spontaneously. If the sinuses or fistulæ thus formed communicate with the mouth, one finds in the discharge granules appearing as minute sand grains or pinhead-sized, sulphur-like bodies. If fever is present it is due to secondary infection; in fact, the clinical picture and the pathologic process are influenced in no small way by infection with the pyogenic organisms. This complication eventually occurs almost invariably, so that the disease may become converted into a chronic pyemia. The connective-tissue proliferation following the earlier granulation-tissue formation changes the boggy nature of the swelling into one of a dense and board-like hardness. The bones of the jaw may be involved simply by a continuity of the infection, leading to an osteoperiostitis with marked thickening, or sinuous tracts may extend to the central cavity and an osteomyelitis with necrosis and sequestration result. From these sinuses small portions of bone may con-

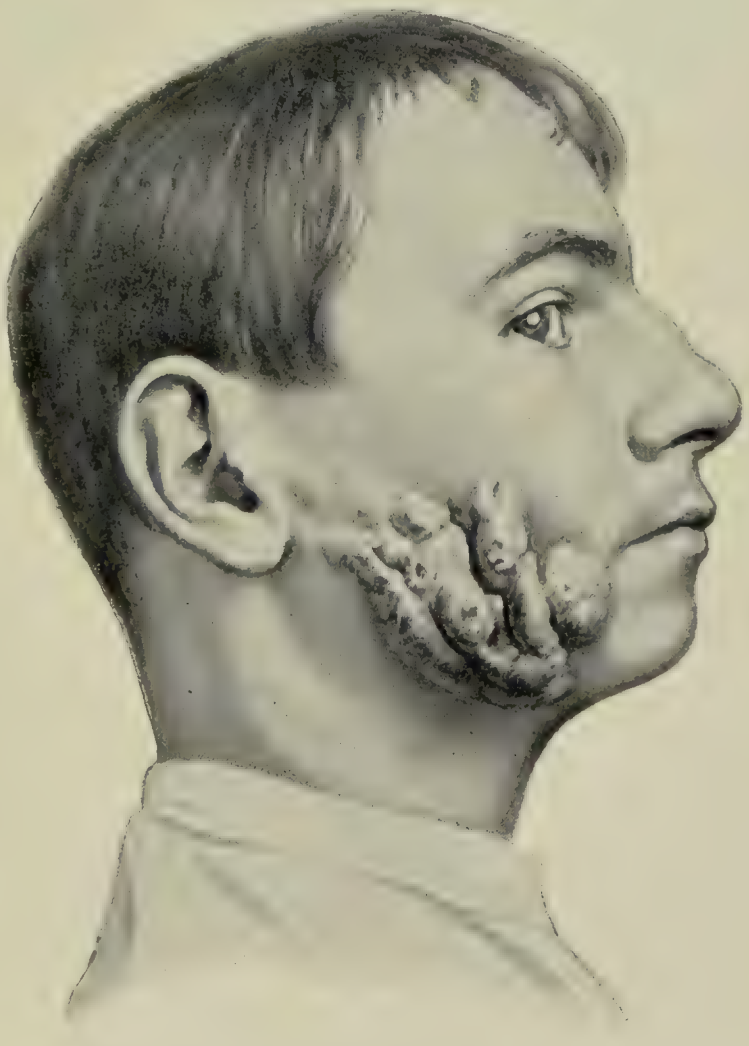


Fig. 140.—Actinomycosis of the Cheek (Illich).

stantly be discharged despite energetic efforts at currettement. A few cases have been reported when the actinomycosis seemed to originate in the center of the lower jaw. Baracz observes, however, that the bones are never primarily attacked either in man or animal. In neglected cases the disease may extend downward along the sternocleidomastoid to the clavicle, involving all the structures of the neck and resembling somewhat a tuberculous adenitis. If the prevertebral fascia is penetrated the discharge, and consequently the disease, may travel downward into the posterior mediastinum. In other cases, particularly those originating in the upper jaw, the antrum of Highmore is easily invaded, and as the disease works upward the base of the skull may be reached and meningitis or abscess of the brain occur.

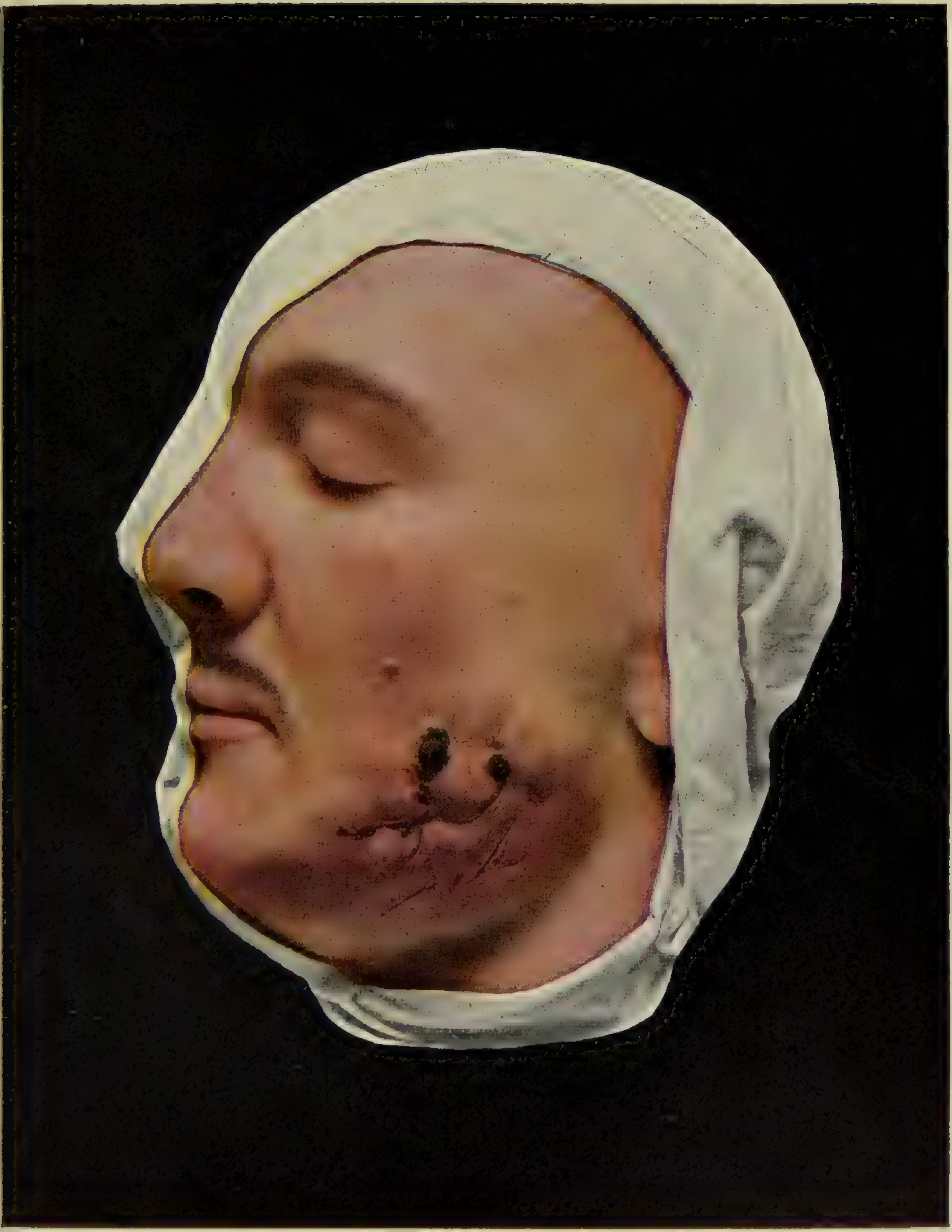
Actinomycosis of the tongue is observed occasionally and begins as a nodule, which later undergoes ulceration. The nodule is hard, situated beneath the mucous membrane, is not freely movable, and may persist for months before it softens and breaks down. Actinomycosis of the salivary glands from infections through the ducts has been observed, and the thyroid may be affected by extension of the infective process. Several cases have been reported in the lacrymal ducts.

Cerebral actinomycosis is not common, Howard,[31] in 1903, collecting only 5 primary and 13 secondary cases. These included under the term actinomycosis, infections by allied organisms such as streptothrix and cladothrix. If the latter were excluded, there would remain but 1 primary (Bollinger[32]) and 8 secondary cases. The condition is recognized in the brain by the presence of an abscess containing the actinomycotic granules, and the symptoms correspond to those of an acute abscess of the brain. Mueller[35] observed yellowish-white patches in the retina of both eyes due to miliary actinomycosis. Enriquez and Sicard[33] have reported a case of primary cerebral tumor in which lumbar puncture revealed the characteristic granules with central mycelium and peripheral club-shaped bodies.

2. **Thoracic actinomycosis** is characterized by a cough with more or less profuse, often fetid expectoration; by fever, which is usually present and often the first symptom; by severe pain over the affected side, continued and increased by respiration, occasionally accompanied by chills and sweating, and finally by progressive emaciation. The ribs, sternum, vertebræ, or opposite lung may be attacked, secondarily, the pleura or pericardium may be filled with pus, and abscesses may form in the cellular tissues; the skin may be riddled with sinuses. Hodenpyl[30] collected 34 cases of pulmonary actinomycosis, of which 32 died. The average duration of the disease in these cases was ten months.

3. **Abdominal Actinomycosis.**—Every authentic case of actinomycosis of the abdomen has arisen from the gastro-intestinal tract. In 50 to 60 per cent. of cases the primary focus was in the cecum, the contiguous portion of the colon, the appendix, or the terminal portion of the ileum. The stomach or small intestine is rarely affected, and the rectum in from 10 to 15 per cent. of cases. In the remaining cases the primary site has not been definitely determined. The early symptoms are so indefinite that an accurate diagnosis is at first impossible. The tumor

PLATE XI.



Actinomycosis (Jacobi).

may not appear for weeks or months after the onset of the disease, which is ushered in with nausea, vomiting, and diarrhea or constipation. In other cases the tumor may be the first sign of the disease, or the case may be regarded as a recurrent appendicitis and the true nature of the lesion not discovered until exposed at the operation. The tumor manifests itself as an irregular, indistinct, tender mass, rarely accompanied by pain, and most frequently appearing in the right iliac fossa or in the umbilical region. After a time the skin over the tumor becomes reddened or bluish and eventually breaks down. Fistulæ form and discharge a grayish serous or purulent fluid with a fecal odor. When the rectum is the seat of disease, sinuses and fistulæ form about the anus, over the buttocks, or occasionally above Poupart's ligament near the iliac crest or pubes.

4. **Cutaneous Actinomycosis.**—Primary infection of the skin is of rare occurrence, occurring only in 2 per cent. of the cases collected by Ruhräh. Leser,[25] who observed 3 cases, concludes that there are two forms: (1) a discrete, nodular form with central cicatrization and peripheral growth as in lupus; (2) an acute ulcerating form which may show necrosis in one part and a dense, hard, granular infiltration in another. There is nothing in the manifestations of cutaneous actinomycosis peculiar to the skin; there is the usual ill-defined, slowly increasing swelling, hard, indurated, often board-like, followed by fluctuation and the formation of sinuses or of a ragged ulcer with undermined edges. The discharge becomes seropurulent and usually contains the typical sulphur granules. If cicatrization takes place in portions of the affected tissues there may be felt one or more "strings" beneath the skin, branching out from the necrotic area. There is no glandular involvement and but little pain. In an interesting case recorded by von Bergmann[34] a man had been kicked in the knee by a horse, the wound was slow in healing, and a swelling persisted, at first with numbness, later with pain. He was treated for several years for osteomyelitis, and it was not until the fifth year that the case was finally recognized as actinomycosis.

Diagnosis.—A positive diagnosis of actinomycosis can be made only by finding the characteristic granules in the pus and the ray fungus under the microscope. Actinomycosis has certain peculiarities, which, however, are of some importance in studying the clinical aspects of a given case. Though the train of symptoms is influenced by the region or tissue affected, the slow and progressive nature of the affection, extending often over a period of months, is in all cases a characteristic feature. An indurated swelling, of wooden hardness and yet elastic, with trismus if situated at the angle of the jaw, and later the crater-like openings are most suggestive. Bevan[27] states that the pus has a distinct odor, resembling that of freshly turned over soil. If pain is present, it is not the characteristic throbbing pain of an ordinary abscess, nor does an incision relieve the pain, as in ordinary abscess. Furthermore, the abscesses of actinomycosis when opened are found to contain but little pus as compared with the amount of diseased tissue. Sarcoma does not cause trismus, the swelling increases more rapidly and is finally of larger proportions, there is no suppuration, and softening is almost always associated with hemorrhage. A differential diagnosis from gummata is sometimes very difficult, and may depend upon the finding of tertiary lesions in other portions of the body. The base of the syphilitic ulcer is ragged and of a dirty yellow color, the actinomycotic ulcer is undermined, filled with flabby granulations, and connected by sinuses with abscess cavities. The surrounding tissue is infiltrated and contains hard strands of tissue. Under large doses of potassium iodid the gumma should be reduced in size in the course of a few weeks, while in actinomycosis the response to the same drug is much slower. Tuberculosis is also difficult to differentiate at times from the actinomycotic lesion; it usually begins, however, in situations in which lymph nodes abound, as in the neck, the axilla, or the inguinal region. In tuberculosis, metastasis or regional infection always occurs through the lymphatic trunks and nodes; this is almost never the case in actinomycosis. The differential diagnosis of an ulcerating carcinoma has been attended with some difficulty in a few cases, particularly because the "epithelial pearls" both in size and shape may be suspiciously like the granules. The microscope will determine their character. Actinomycosis of the cheek, anterior to the masseter muscle, may resemble an inflamed sebaceous cyst (Lexer[28]), but the lesion is usually small and well circumscribed, and the resultant ulcer lacks the usual infiltration. The mucous membrane of the cheek should be examined, and a hard strand may be felt beneath the skin, leading from the skin to the primary focus.

Prognosis.—Actinomycosis pursues a slow course, extending over months and even years, and the expectation of life and mortality are influenced chiefly by the location of the disease. In the abdomen, lung, and brain the process is more rapid than on the skin or about the jaw. The association of the pyogenic bacteria may produce a pyemia and increase the severity of an infection, which, if uncomplicated, might have been amenable to treatment. Some cases recover spontaneously only after surgical intervention. The death-rate of the reported cases in the United States is 47 per cent. Jiron[29] gives the mortality of the various forms as follows: face and neck, 11 per cent.; thoracic, 83 per cent.; abdominal, 71 per cent.; cerebral, 100 per cent.

Treatment.—The treatment may be said to be medicinal, hygienic, and surgical. Just as in tuberculosis, the patient should be surrounded with the most favorable hygienic condition—fresh air, sunshine, and a liberal and nourishing diet. It is not necessary to remove all the diseased area completely, and one should not attempt it unless this is small and well circumscribed. Every suppurating cavity and sinus should be thoroughly laid open and the granulation tissue produced by the lesion should be curetted away. The wound should then be thoroughly swabbed with nitrate of silver in stick or solution (10 per cent.). If extensive masses of cicatricial tissue must be left, they should be injected with carbolic acid solution (5 per cent.). The wound should be kept open with iodoform gauze and the curetting and cauterization repeated as often as relapses occur, one or more always occurring. Internally the patient should be given potassium iodid in maximum doses, not continuously, but for periods of a week at a time, with intervals of four to five days. This drug seems to have a specific effect in those cases uncomplicated by secondary infection. The thoracic cases do badly and can only be treated as the lesion appears upon the surface of the body or upon involvement of the pleuræ. Potassium iodid seems to have less effect in this class of cases than in the others. Sawyers[29] successfully treated one case by injection of ʒss of potassium iodid (1 per cent.) directly into the lung at the point of greatest dullness, every third day. Surgery may be of some benefit when actinomycosis attacks the abdominal organs; unfortunately the nature of the disease is not usually recognized until radical extirpation of the disease is out of the question. The peritoneal cavity should be opened, explored, and perhaps irrigated with a normal saline solution. Precaution must be taken to protect the general peritoneal cavity and, as Ruhräh[25] observes, one must be on the lookout for a rather profuse and uncontrollable hemorrhage, if many adhesions have been separated in the course of the operation. The appendix if diseased should be removed, together with any masses of granulation tissue in the right iliac fossa. Fistulæ and sinuses must be followed up and treated as the occasion may require. If a secondary abscess of the liver is diagnosed, it must be opened and drained by way of the abdomen, the thorax, or the loin. Bevan[37] has recommended the internal administration of cupric sulphate, in doses of from one-fourth to one-half a grain, increasing the dose if necessary to one grain, three times a day, and irrigation with a 1 per cent. solution.

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MALIGNANT EDEMA.

Synonyms.—Emphysematous Gangrene; Gangrène Foudroyante; Gaseous Phlegmon, etc.

Definition.—A rapidly spreading gangrenous inflammation, caused by certain specific microörganisms, characterized by a gaseous infiltration of the tissues and a profoundly rapid intoxication.

Historical.—Maisonneuve[1] in 1853 wrote a classic clinical description of gaseous phlegmons under the name of "gangrène foudroyante." Pirogoff[2] in 1864 described the same process, calling it "primary mephitic gangrene" or "acute gangrenous edema." Bottini[3] in 1871 showed the infective nature of the disease. The bacillus of malignant edema was first described in 1877 by Pasteur[4] as the "vibrion septique." Several years later Koch and Gaffky[9] found the same organism in the human body and called it the "bacillus of malignant edema." After these publications many instances of emphysematous gangrene were reported, all of which were attributed to the organism of Pasteur or of Koch. In 1891 Welch and Nuttall[5] discovered a bacillus in the blood and tissues of a man dying from the rupture of a thoracic aneurysm and termed it the "Bacillus aërogenes capsulatus." Fraenkel[6] in 1893 reported an organism found in fatal phlegmons, "the Bacillus phlegmones emphysematosæ," which, however, is identical with the Bacillus aërogenes capsulatus. Welch[7] in a later communication remarks that in very few of the alleged cases of malignant edema in human beings were the descriptions or cultural methods sufficiently exact satisfactorily to identify the infection as being one due to the genuine malignant edema bacillus. The most common and important specific cause of gaseous phlegmons or emphysematous gangrene is the "Bacillus aërogenes capsulatus." Welch also considers it an unsettled question as to whether the bacillus of malignant edema can produce an identical or similar anatomic and clinical affection in human beings. For the present, at least, they can be considered as producing the same clinical picture. Some observers attribute cases of gaseous phlegmon to the colon or proteus bacillus. Welch doubts the accuracy of the findings, although recently Dudgeon and Sargent[23] report a case definitely due to a member of the Bacillus coli group.

Etiology.—Gas bacilli are found as natural habitants of the soil, and, in the case of the Bacillus aërogenes capsulatus, at least, also in the intestinal tract of man and other animals. It has also been found by

Walker[8] in dust collected by sweeping floors, and by Harris[10] in an old cesspool. Welch remarks that it must occasionally be present upon the human skin. These gas bacilli may produce lesions of many portions of the body, the majority, however, being a result of severe injuries, especially crushing wounds of the extremities. Koenig[11] states that there is a frequent history of the organism having been "forcibly pressed into the wound." This, of course, is in accord with its anaërobic method of growth. Compound fractures and gunshot wounds, especially when followed by infection, are the most frequent lesions. Thus, in a recent case reported by Trimble[14] the gaseous phlegmon followed a fracture of the middle of the femur, the end of the bone having been embedded in the ground. Chisholm[15] treated a patient in whom malignant edema of both hands followed a dynamite explosion. In 5 cases (10.9 per cent. of 46) collected by Welch, infection with the Bacillus aërogenes capsulatus followed hypodermic injections and infusion of normal salt solution in patients in a state of marked depression. In other cases, as in those following appendectomy, herniotomy, nephrectomy, urethral injuries, emdometritis, etc., the source of infection is believed to be the intestinal tract. The circulation may deposit the bacilli in tissues whose vitality is impaired through trauma, as in the cases recorded by Bloodgood,[12] Soupault and Guillemot.[13]

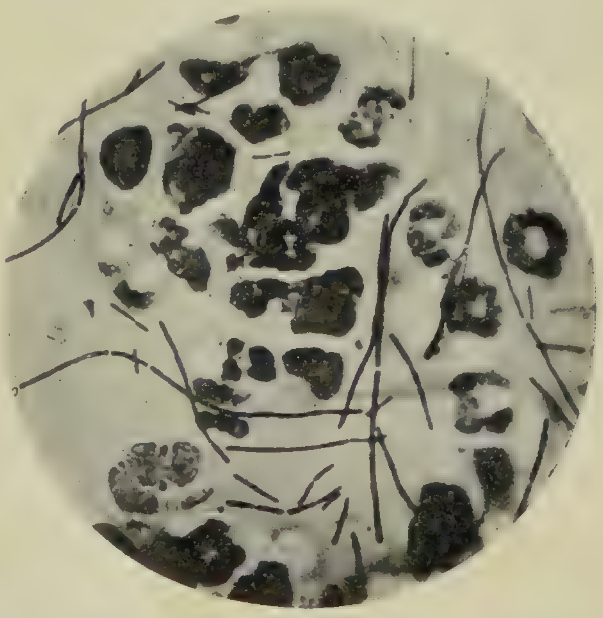

Fig. 141.—Bacillus of Malignant Edema from the Body-juice of a Guinea-pig Inoculated with a Bouillon Culture. × 1000 (Fränkel and Pfeiffer).

Pathology.—Post-mortem examination of the tissues within a few hours after death reveals a gangrenous necrosis, a diffuse edema, or the presence of gas-bubbles in the tissue spaces and an exudation of bloody serum. The nuclei disappear by karyolysis and there is an absence of the leukocytic infiltration seen in ordinary infections. The blood, particularly in the veins and the organs, may contain gas-bubbles and the pulmonary vessels fat emboli. If a distinction could be made without bacteriologic investigation, malignant edema will probably be indicated by a gangrenous necrosis with hemorrhagic edema and without suppuration or gas-bubbles. The latter phenomenon is characteristic of infection with Bacillus aërogenes capsulatus, although this organism has been isolated from certain organs, small abscesses, the gall-bladder, etc., without the production of gas and with suppuration. These infections are usually associated with infections by various pus-producing organisms, especially the streptococci and staphylococci; the mixed infection increases the purulent nature of the lesion without altering to any marked degree the pathogenic properties of the gas bacillus.

Symptomatology.—Most of the recorded cases of gaseous emphysema have followed gunshot wounds or compound fractures. In a few hours, usually twenty-four to forty-eight, there is noticed about the point of injury a diffuse swelling of the tissues, which become livid in appearance and upon palpation yield a fine crepitus. The secretion from the wounds is reddish or brownish, acrid, foul-smelling, and, as a rule, contains bubbles of gas. The overlying cuticle may be raised into blebs containing bloody serum. The onset of the disease is marked occasionally by chilly sensations, by a feeling of tension in the wound, and by a rise in temperature. If the wound is opened the muscles are found to be pale, necrotic, and separated from their aponeuroses by an exudate hemorrhagic, necrotic, and containing bubbles of gas. The tissues may be intensely edematous or emphysematous, the patient becomes profoundly prostrated, and in the majority of cases succumbs to the overwhelming toxemia. The process extends to the surrounding tissues with amazing rapidity.

Diagnosis.—Cover-slips of the secretions should be made from every wound exhibiting the characteristic features of this condition, namely, emphysema and edema, the preparation stained by Gram's method, and the presence or absence of the gas bacilli determined. The rapid appearance of hemorrhagic edema, the dusky appearance of the skin, the rapid extension of the process, and the presence of the gas-bubbles in a foul, hemorrhagic secretion, suffice to differentiate malignant edema from erysipelas.

Prognosis.—The prognosis in all cases of malignant edema is most grave, the disease in most instances leading to a rapidly fatal termination. Welch [17] in 46 cases found the mortality to be 59 per cent. The prognosis depends somewhat upon whether the tissues of the trunk or the tissues of the extremities are affected, and whether the condition is recognized promptly and energetic treatment applied without delay. In the case of the extremities, a prompt amputation of the limb will often save the patient's life. As a rule, death is due to the profound toxemia although in some cases it has been attributed to gaseous embolism. In a few of the reported cases just about the time that the patient was recovering from malignant edema tetanus developed and led to a fatal termination, the difference in the incubation period of the two organisms accounting for the difference in the time of onset of the two diseases.

Treatment.—To be effective the treatment must be vigorously applied and without a moment's delay. In the case of the tissues of the trunk free incisions should be made in order to afford an outlet for the toxins, and in order also to enable one to bring the disinfecting solutions into immediate contact with the tissues. In the case of the extremities, if the condition is recognized in its early stages and is not very extensive the symptoms may subside after free incisions are made and the affected tissues subjected to the continuous irrigation or the continuous bath. If the relief is not prompt and decided, the surgeon should proceed without hesitation to amputate the limb, and always far enough above the invaded tissues to enable him to make the incisions through healthy tissue. There are cases in which the process extends with such astounding rapidity that the surgeon will realize in an instant that nothing short of instant amputation will save the patient's life. For purposes of irrigation Fraenkel,[18] Muscatello and Gangitano,[19] Koenig,[20] and other writers have recommended oxidizing solutions such as those of potassium permanganate or hydrogen dioxid, because of the anaërobic character of the offending bacilli. Lotheisen[21] suggests injections and continuous irrigation with hydrogen peroxid, though, with Hitschmann and Lindenthal,[22] he is inclined to believe that amputation offers the best chance of recovery. Stimulants should be administered liberally as supportive measures to counteract the exhausting effect of the toxins.

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CHAPTER XIV.

DISEASES DIRECTLY DERIVED FROM ANIMALS, INSECTS AND REPTILES.

By Charles Harrison Frazier, M.D.,
PHILADELPHIA.

HYDROPHOBIA.

Synonyms.—Rabies; Lyssa; Hundswuth; Rage.

Definition.—An acute infectious disease of the central nervous system, of unknown origin, communicated from animals to animals or from animals to man by the bite of an affected animal and productive of symptoms resulting fatally.

Historical.—Rabies has been a dreaded disease from the earliest dawn of history, exciting terror and horror whenever occurring and having a veil of mystery, superstition, or doubt cast over its occurrence and symptoms. There are many references supposed to indicate that the disease was known among ancient peoples. Thus Homer mentions the dog-star, or Orion's dog, as exciting a malignant influence upon the health of mankind. Aristotle[1] (322 B. C.) is credited with a clear description of the disease, and he asserts that the human species is exempt from infection by animals. During the early centuries of the Christian era Celsus,[2] Pliny,[3] and Pontus Ægineta,[4] among others, wrote upon the affection and described its forms. At the commencement of the eleventh century Avicenna,[5] an Arab, wrote a very complete treatise upon the treatment of rabies, and states that its victims barked like a dog and were often suffocated in attempting to drink. In 1026 the first record exists of its presence in England. Other writers wrote of the disease, although the prevention and treatment were obscured by superstitious rites and ideas. Many early records exist recording the transmission of rabies to man by animals, wolves being the most frequently mentioned, and in England Huxham[6] in 1735 speaks of "many mad dogs running up and down" in August. The disease then seems to have spread over the whole of Europe, and in 1768 rabies is said to have been alarmingly frequent in Boston and other towns of North America.[7] In 1779 it appeared in Philadelphia and in Maryland, and in 1785 was prevalent all over the Northern States and spreading to the South. In 1860 rabies again was prevalent in America, especially in the west.

In 1804 Zinke[8] demonstrated by experimentation the inoculability of animals and the virulence of the saliva of rabid dogs. Gohier[9] in 1811 observed that the carcasses of dogs dead from rabies were capable of causing infection, and Grüner[10] in 1813 showed by experiment the infectiousness of the saliva. In 1879 Galtier[11] described the disease in rabbits, and in 1883 Paul Bert[12] showed the particulate nature of the virus of rabies. In 1881 Pasteur[13] began his series of observations which placed the disease upon its present basis, because he demonstrated the existence of the poison of rabies in the central and in the peripheral nervous system. Later he showed that the previous difficulty in inoculating rabies was due to the failure to inoculate the virus into the nervous system, and in 1884 he obtained the attenuation of the virus which in 1885 was applied to the method bearing his name used in the treatment of the disease.

Etiology.—Rabies is fairly prevalent in almost every country on the globe, Australia and Norway being notable exceptions, and at the present time it is very rare in England, owing to strict laws relating to the importation of dogs. It is most common in France, Belgium, and Russia, wolves being frequently affected in the latter country. Salmon, in the vital statistics of the census of 1890, records 143 deaths from 30 States in this country. Rabies or hydrophobia in man is contracted in nearly nine-tenths of the cases from dogs, sometimes from cats or wolves. All mammifers are liable to the disease, cattle, sheep, goats, foxes, hyenas, and jackals more especially, together with the others first named. It is rare in the horse or in swine, in the latter supposedly because of the large amount of subcutaneous fat. It occurs in birds, Kraus and Clairmont[14] noting changes in the central nervous system analogous to those found in man and the higher animals. The disease is more prevalent in males; two-fifths of the cases are under fifteen years of age. The season of the year is not of great moment, but Salmon[15] in a total of 14,000 cases found June to be the highest month, and though there were more cases reported from April to September, yet the difference is not sufficient to be of etiologic importance. All persons bitten by rabid animals do not develop hydrophobia, Bradford[16] estimating that from 10 to 20 per cent. contract it. The danger of infection varies with the animals inflicting the bite, the wolf, cat, dog, and other animals being relatively dangerous in the order named. Bites upon exposed parts are more dangerous than those in which the virus may be removed by the passage of the teeth through the clothing. The greater the nerve-supply and the higher the wound, those about the face being most dangerous, the greater is the chance of infection. Sometimes immediate cauterization has probably prevented the later development of the disease. The ordinary medium of infection is the saliva of the rabid animal, although certain of the fluids and tissues of an animal so affected when inoculated may produce the disease. It is very probable that a microörganism is the causative agent, although as yet this has not been satisfactorily demonstrated. Gibier,[17] Pasteur,[18] Roux,[19] Fol,[20] Babés,[21] A. Bruchettini[22] and others, and more recently Negri[23] and Levy,[24] have announced the organism, but have failed to obtain confirmation of their supposed discovery. The organism is probably similar to that of tetanus, and the more recent one of Negri has attracted considerable attention. The period of incubation varies greatly and is probably directly dependent upon factors just mentioned—the part bitten, the variety of animal, the susceptibility of the patient, and the virulence of the virus. Ravenel[25] places the average incubation period in man at forty days and in dogs from twenty-one to forty days. Bradford[16] states that it is probably unknown after six months, while Gowers[26] and others believe that the disease has developed after a year or eighteen months. A few years ago a case of hydrophobia was reported[27] that presented the first symptoms seven months after the Pasteur treatment had been carried out, the diagnosis being confirmed by animal inoculations.

Pathology.—The macroscopic changes shown at necropsy are not characteristic, the brain, cord, and their membranes often being normal in appearance. Marked lividity of the dorsal surfaces, and a thick, dark state of the blood are characteristic of the insufficient aëration present before death. The mucous membranes, particularly of the respiratory tract, are catarrhal, the seat of hyperemia and hemorrhagic areas, and frequently covered with a frothy, dirty mucus. The internal organs are either normal in appearance or in a state of parenchymatous hyperemia, the kidney being most apt to be so affected. Edema of the brain and congestion of the cerebrospinal system may be demonstrated, the virus of the disease seeming to spend its force chiefly upon the nervous system. Microscopically the changes in the nervous centers are said to consist of hyperemia and dilatation of the blood-vessels, with areas of hemorrhage and a round-cell infiltration both in the sheath of the smaller vessels and in the peri-vascular spaces. The nerve-cells are often degenerated and local areas of softening may be found in different parts of the central nervous system, most markedly in the bulb. Golgi[28] considers the disease to be an acute encephalomeningitis and the areas of softening have been described by Gowers[26] and Kolesnikoff[29] (1875) as "miliary abscesses." In 1886 Babés[30] described the accumulation of certain embryonic cells about the motor centers of the bulb and cord in the neighborhood of the central canal, and in 1892 reaffirmed and laid stress upon the diagnostic value of his observations. These cell accumulations are usually called "Babés's tubercles," and for all practical purposes are identical with the masses described by Kolesnikoff. This rabic tubercle of Babés is not always present, and Van Gehuchten and Nelis[31] and others questioned its value, although Crocq[32] in an admirable review of the subject believes that its presence is of considerable diagnostic value. In 1872 Pollailon and Nepveu[33] noted that the Gasserian ganglion was hyperemic, infiltrated with round cells, and was compressed. Van Gehuchten and Nelis[31] in 1899 and 1900 laid stress upon the importance of the changes in certain of the ganglia and described a round-cell invasion and proliferation of endothelial cells lining the capsules in which the large nerve-cells of the ganglia are placed. The nerve-cells may be entirely destroyed and replaced by the round-cell invasion. The changes are most constant and most severe in the peripheral, cerebral, and sympathetic ganglia, also in the intervertebral ganglia and the plexiform ganglia of the pneumogastric. The lesions of the cerebrospinal and sympathetic ganglion discovered by Van Gehuchten and Nelis have been utilized for the purpose of a rapid diagnosis, and the claims of these investigators have been substantiated, particularly by Degive and Hebrant,[34] Nocard and Vallée,[35] McCarthy and Ravenel.[36] The latter writers in 105 cases of rabies in animals, mostly dogs and rabbits, obtained positive results in 94 by the examinations of the ganglions or medulla. They state that the chief cause of failure is the premature killing of the animal, and that in only one disease have they found lesions liable to be mistaken for those of rabies, namely, "forage poisoning" of horses and cows. Similar lesions to those of Van Gehuchten have, however, been found in the ganglia by Crocq [32] in a case of diphtheria, by Burr and McCarthy [37] in a case of alcoholic neuritis, and by Spiller [38] in a case of acute ascending paralysis and in an endothelioma of the Gasserian ganglion. Marinesco [39] believes that the Bacillus botulismus, which is found in sausage-poisoning, is capable of producing the same changes as those described by Van Gehuchten and Nelis as pathognomonic of hydrophobia.

Spiller [40] concludes that no lesions are specific to rabies; Anglade and Choireaux [41] do not believe that the changes found in the nerve-cells are as diagnostic as regards rabies nor early enough in appearance as compared with lesions of the neuroglia and blood-vessels, and Dadi [42] after investigating a large series of animals does not believe that it is possible to make an absolute diagnosis through the simple examination of the nervous system. The characteristic changes may be absent, though if present Dadi believes they are of the utmost importance in diagnosis. The whole question therefore seems to be unsettled, and moreover the lesions are not well marked in the early stages of the disease and it is only with great difficulty that the ganglia can be obtained. In 1903 Negri [23] described the existence of small bodies or corpuscles usually found as inclusions in the Purkinje cells of the cerebellum and in the large ganglion cells in the region of Ammon's horn, and believes them to be the causative agent of rabies. They are described as protozoa, one to twenty-three microns in diameter, and are readily stained and recognized. Poor [43] places the possibility of error at 5 per cent., and failed to find them in a number of experimental infections, except one case of tetanus where a few minute eosinophile bodies occurring as inclusions in the Purkinje cells of the cerebellum were observed. Poor believes that the recognition of the Negri bodies has accomplished the long-sought rapid diagnosis of rabies. Luzzani [44] reports 455 animals examined by various authors for the Negri bodies, of which 296 were found to have rabies; and of these, 287 enabled a positive diagnosis to be made.

Symptomatology.—After a varying period of incubation the victim complains of lassitude, malaise, loss of appetite, and sometimes slight feverishness. There is often some pain or irritation at the seat of the wound, sometimes referred in the centripetal direction of nerve or blood-vessel. The patient becomes nervous, irritable or worried, particularly if he recalls the former injury, and may wander aimlessly about during the daytime and suffer from sleeplessness at night. The pulse may be accelerated, the face alternately flushed or pallid, and hypersensitiveness to currents of air and to light be noted. This early stage is that of irritation and lasts two or three days, at the end of which time the second stage, that of excitement, is introduced by more or less difficulty in swallowing and stiffness of the muscles of the neck. Excitation of the mechanism of swallowing by attempts to relieve thirst are followed by spasms of the glottis, neck and jaw muscles. Water produces the most marked reflex, but semisolids or solid food may also induce spasms, which in a short time become generalized convulsions. Increasing anxiety and expectation of death characterize the mental conditions; and periods of hallucinatory delirium ensue in the intervals between convulsions. In two or three days death may occur from exhaustion or heart failure or the patient may pass into the third or paralytic stage. Rapidly ascending paralyses are observed, beginning in the lower extremities, later involving the upper, the pulse becomes weak, respiration hurried, and invasion of the pons and pneumogastric failure terminate the patient's life. The paralytic stage rarely lasts more than twenty-four hours, and rarely the muscular spasms may be slight or absent, the paralytic symptoms alone being present, constituting the *dumb rabies* so commonly seen in dogs.

Diagnosis.—Hydrophobia must be distinguished from pseudo-hydrophobia, a hysterical condition simulating the true disease, from tetanus, and from certain manifestations of epilepsy and hysteria. Pseudo-hydrophobia may very closely resemble the real condition and even proceed to a fatal termination, particularly in patients bitten by a dog and who are of a highly excitable and imaginative disposition. Great care must be taken to differentiate the two conditions, and certain symptoms characteristic of the pseudo-disease should be remembered. A very short period of incubation is suspicious and is an absolute sign if the symptoms occur a day or two after the receipt of the bite, because hydrophobia never appears within five days of the injury and rarely within a week. The absence of premonitory symptoms and the immediate occurrence of the convulsions, particularly when accompanied by barking, growling, or snapping, in imitation of a dog, are also suggestive of pseudo-hydrophobia. The pharyngeal spasm will not spread into the respiratory muscles and the throat can be easily examined with a tongue depressor. If the symptoms persist for ten days or if recovery takes place, the proof is absolute.

In tetanus the cause is a wound, not a bite; the spasms are tonic in character and affect the muscles of mastication, and not those of deglutition. The incubation period is shorter, there is no terror, no remission between the convulsions, and the respiratory embarrassment is not due to spasm of the laryngeal muscles.

Prognosis. — The prognosis has been invariably fatal once the symptoms have appeared.

Treatment.—**Prophylaxis.**—The immediate treatment of a bite from any animal is of great importance, particularly if situated upon the face or upon an exposed bare surface of the body. Cabot [45] believes the unknown microörganism to be fermentative in character, lying localized for at least twenty-four hours and then infecting the system by way of the nerves and not directly by the blood. Moreover, Babés [46] has shown that while the disease may not be prevented by excision or cauterization, the period of incubation is lengthened, thus favoring the success of Pasteur's treatment.

Excision of a wide area about the part bitten, followed by disinfection of the wound, should be performed if at all feasible. If excision is not possible by reason of the location of the bite, the wounded area should be scrubbed with a brush and green soap, followed by bichlorid of mercury (1:1000), with as much care as is taken in the preparation for an abdominal operation. After anesthetization, general or by cocain, the wound should be thoroughly swabbed with pure carbolic acid, followed by fuming nitric acid applied with a pointed glass rod (Cabot). The thermocautery and silver nitrate may also be used, but are not as efficient as nitric acid.

Preventive.—Since 1885 the Pasteur treatment has been applied to human beings bitten by rabid animals, and the success of the method justifies the statement that in all cases of bites from rabid animals the patient should be subjected to the inoculations at the earliest possible moment. The principle of treatment is comprised in the establishment of an immunity during the period of incubation, and consists in the inoculation of a virus of graded potency present in bits of the spinal cord of rabbits. Since the commencement of the Pasteur preventive treatment some 55,000 persons have been inoculated, with an average mortality of 0.77 of 1 per cent. (Ravenel [25]).

Serum Therapy.—Babés and Lepp [47] in 1889, Tizzoni and Centani [48] in 1895, describe a serum which has been used with great success in the treatment of experimental rabies in rabbits.

Treatment with Radium.—Tizzoni,[49] recently, states that the radium rays have a rapidly destructive action on the fixed virus of rabies in the test-tube, and he found it possible to cure rabbits by radium exposures even after the fifth day when the disease had passed through four-fifths of its course. He calculates that man would require four to six million radio-active units. Calabrese [50] experimentally concluded that the Röntgen rays have no effect upon the virus of this disease.

Rabies of the Dog.—There are two types in rabies of dogs, the furious and the paralytic forms, the latter often being referred to as "dumb rabies." Gill [51] succinctly states the early appearance of suspicious symptoms in the following words: "Beware of a dog when it becomes dull and hides away, appears restless, always on the move and prowling; whose countenance is somber and sullen, walks with head down like a bear. Beware of one who barks at nothing when all around is still. Beware of a dog that scrapes incessantly and tears up things. Look out for the dog which has become too fond of you, and is continually trying to lick your hand and face. Beware, above all, of the dog who has difficulty in swallowing, which appears to have a bone in his throat, and one that has wandered from home and returns covered with dirt, exhausted and miserable."

The dog, if at all possible, should be kept alive and under observation for a week. If it remains well, there is no rabies; and if it dies, the nervous tissues show certain changes which are worth something, Cuillee and Vallee [52] having shown that in dogs experimentally inoculated the changes may not be found if the animal is killed early.

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BITES AND STINGS OF INSECTS.

The rôle which insects play in the spread of disease has long been suspected, and during recent years has been better recognized and become a subject of practical importance. Malaria, yellow fever, elephantiasis, sleeping fever, relapsing fever, Texas fever, typhoid fever, tuberculosis, plague, Asiatic cholera, yaws, leprosy, and anthrax are the important diseases in which insects, particularly the mosquito and fly, are believed to play an important part. The discussion of the elimination of the insect as an agent in the spread of these diseases belongs to the domain of preventive medicine and not to surgery, although their influence should be remembered as a very possible factor in the dissemination of infection from a suppurating to a clean wound. In all hospital wards and dressing-rooms care should be taken to keep bedbugs, flies, ants, moths, etc., from obtaining access to wounds.

Bites and Stings of various insects are productive of local inflammations from the injection of some poisonous secretion from distinct poison glands of the insects inflicting the minute punctured wound. As a result of the injection of this poison various phenomena result, varying from simple local irritation to severe phlegmonous inflammations and even death. The minor degrees of irritation are produced by flies, house-fleas, gnats, mites, bedbugs, mosquitos, etc. The swelling produced by these insects, while sometimes diffuse, usually reaches its height in a few hours and is not progressive in character. A few severe cases have been reported, Paltauf [1] observing erysipelas, meningitis, and death in two days from a fly-bite, and Joseph [2] reporting three cases of septicemia due to fly-bites. It is probable that in these some vegetable organism was introduced into the wound by the insect. Moore [3] reports such a case in a girl of eight years of age who was bitten on the right side of the nose and on the orbital margin. She died two and a half days later with symptoms of marked orbital cellulitis, 104.4° F. temperature, pulse about 200 beats in a minute, twitching and rigidity of arms and legs, and photophobia. At necropsy a primary focus of suppuration was found in the cellular tissues of the lower lid, pyemic infarcts in the left lung, and pleural and pericardial effusions. Bacteriologically, there was a general infection with staphylococci.

Treatment.—The use of a carbolic-acid soap for washing purposes is an excellent preventive when working where insects are numerous. For the bites, alkaline local applications, such as a solution of sodium bicarbonate or weak ammonia water, camphorated menthol, pure ichthyol, or a saturated solution of camphor or salol in ether, may be found useful. Local inflammatory reactions must be treated on general principles and the rare constitutional disturbances by appropriate stimulants.

Hymenoptera, such as *bees*, *wasps*, *hornets*, and *yellow-jackets*, frequently cause stings with severe or even grave symptoms. The sting of a bee is barbed and is consequently left in the wound, while that of a wasp is pointed, thus enabling the insect to sting more than once. Following such stings, intense throbbing pain is experienced; and if the sting is inflicted where the skin is thin or where there is an abundance of loose subcutaneous tissue, marked swelling quickly arises, the skin becoming tight and of a mottled red color. The swelling very rapidly becomes diffused, and if stung on the finger the whole hand and even the arm may be involved in a few hours; if on the eyelid, the eye is closed; or if on the lip, a swelling three or four times the normal size is observed. The latter appearance has been popularly ascribed to a mythical "kissing bug." In a case reported by Parry [4] a patient was stung on the finger by a wasp, and in a few minutes general urticaria resulted, causing intolerable itching, vomiting, a subnormal temperature, and an excess of phosphates in the urine.

In the great majority of cases the results of these hymenoptera stings rapidly subside under almost any local treatment, but occasionally serious complications have been reported. Among the immediate general symptoms observed are syncope, nausea, vomiting, diarrhea, and a rapid irregular pulse suggesting shock; and later edema, septicemia, erysipelas, phlebitis, pyemia, etc. Cooke [5] reports a case where death from syncope occurred twenty-five minutes after being stung; Marquie,[6] Fabre,[8] and others [7] also report fatal cases. Fabre describes a dozen cases followed by severe disturbances of the respiratory, digestive, nervous, and secretory systems, and states that the action of the poison is frequently more subtle and more rapid than that of snake or viper venom, which it closely resembles.

Hodenpyl [9] has reported two cases of cutaneous spindle-cell sarcomata developing after a sting of a wasp. In one, a man of forty-six years, stung over the sternum, the tumor developed immediately and slowly in size. It was removed two years later. The second also developed immediately and on the thumb of a man sixty-three years old, and was removed three months later. Wooley [10] observed a squamous-cell carcinoma of five months' duration on the forearm of a man fifty-four years old which had followed the bite of a green fly.

Treatment.—Do not squeeze the wound until the blister has been carefully opened and the barb extracted. The venom, being acid in reaction, is neutralized by vinegar water, dilute ammonia water, or a solution of bicarbonate of soda. These, together with the ordinary mud poultice, are familiar and long-used popular remedies. In severe cases local treatment on general principles should be used, lead-water and laudanum being very efficacious, supplemented by a hot drink containing some diffusible stimulant when the victim is a child or a nervous individual. Active treatment must be pursued if constitutional symptoms appear, so directed that the elimination by kidneys, skin, saliva, and intestines is increased.

Centipedes, spiders, scorpions, tarantulæ, may inflict severe and even fatal wounds, especially in those weakened by fatigue, malaria, or the abuse of alcohol. The common centipede is harmless, the venomous variety having single pairs of short legs to each segment of its flat body. These insects are common in the tropics or in hot portions of the temperate zone, and the effects of their bites are for the most part local and of varying intensity, although constitutional effects have also been noted rather frequently, usually of an erysipelatous nature. Spiders may produce ulcerations which obstinately resist treatment. Scorpions and tarantulæ are often exceedingly venomous, and Maus [11] reports a variety of the former, a native particularly of Mexico, which causes death in many cases. The symptoms in brief are itching, formication, violent sneezing and expectoration, irregular muscular contractions of the legs and arms and trismus, congestion of the conjunctiva, gastro-intestinal and respiratory systems, and death from asphyxia or pulmonary congestion.

Bot-flies, gad-flies, sand-fleas (jigger or chigo), ticks, etc., occasionally deposit their eggs beneath the human skin or, as in the case of the last two mentioned, burrow beneath the skin and produce severe ulcerative lesions. The bot-fly rarely causes trouble to man. Oviposition from the gad-fly occurs without the knowledge of the victim, and, according to Walsh,[12] after an incubation period of a week or ten days pain, redness, and swelling are noted at the location of the parasite and a tense boil or furuncle develops with an increase in the size of the inflammatory area. In untreated cases deep abscess may result. The insect is common in South America, Mexico, and Central America. The sand-flea, jigger, or chigo, as it is variously called, is most common in the West Indies and other regions lying near the tropics. The female burrows beneath the skin of the host, particularly about the ankles, between the toes, or beneath the toe-nails, and produces great itching followed by a painful swelling. Violent inflammation and even gangrene may result from neglected chigo sores.

Treatment.—The extraction of the parasite and an antiseptic protective dressing is the only treatment necessary unless a deep abscess should require drainage. In the case of the chigo care must be exercised not to rupture the sac, as the liberation of the eggs may increase the lesion originally produced and set up a serious and even fatal inflammation. The use of essential oils on the feet, according to Walsh,[12] may prevent attacks.

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SERPENT BITES.

The great family of snakes, the order Ophidia, is popularly divided into poisonous and non-poisonous snakes; a division, however, of but little practical importance, because the two classes are not separated by any sharply marked characteristics and are often difficult to distinguish even by experts unless carefully examined. Poisonous snakes are widely distributed in all countries of the temperate and especially of the torrid zones. In the United States about seventeen species of rattlesnakes and ten species of copperheads and moccasins, vipers, coral and harlequin snakes, etc., are classed as poisonous; with them a Texan reptile known as the Gila monster is also classed. In South America, Central America, Africa, the West Indies, and Australia, many venomous reptiles are found; the *Hoplocephalus curtus*, or tiger snake of Australia, having been used by Martin in experiments contradicting some of Calmette's assertions. In Europe the adder and viper are dreaded, while in India much attention has been paid to the Thanatophidia, the cobra having furnished the venom upon which the work of Fraser, Calmette, and others has been based.

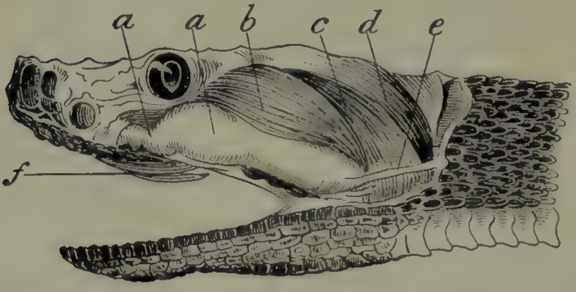

FIG. 142.—MYOLOGY. LATERAL VIEW.
a, *a*, gland; *b*, anterior temporal muscle; *c*, posterior temporal muscle; *d*, digastricus muscle; *e*, posterior ligament of the sheath of the gland; *f*, vagina dentis—the fang slightly raised (S. Weir Mitchell).

Snake Venom.—The appearance of nearly all venom is physically similar—a viscid liquid, varying in color from a straw or greenish yellow to a deep orange or amber, of an acid reaction, and of a specific gravity varying from 1030 to 1070. Venoms dry rapidly to scaly translucent chips resembling egg-albumen and have a distinctive odor. Dried venom apparently keeps indefinitely and in the fresh state is practically free from microörganisms. Putrefaction does not destroy the virulence of the venom.

The composition of venom has been the subject of speculations and experiments for many years, nothing of importance having been attained until by Fontana[1] in 1781. In 1843 Lucien Bonaparte[2] came to the conclusion that the venom of the European viper was albuminous or proteid in nature. In 1861 and 1868 Mitchell[3] published his first experiments, and Fayrer,[4] Lauder Brunton,[5] Richards,[6] and Wall[7] contributed noteworthy papers. In 1886 Mitchell in conjunction with Reichert[8] published a monograph which has served as the foundation for all later studies of snake venom in its action upon the blood and nervous system of animals. They called attention to the loss of coagulability of

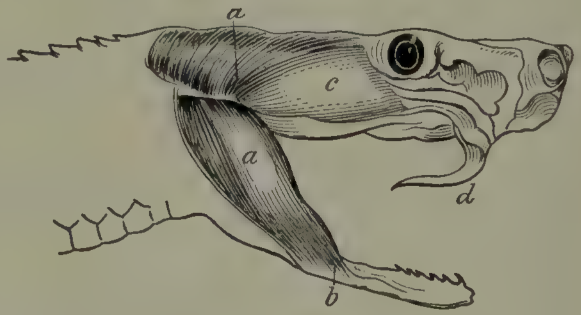

FIG. 143.—EXHIBITING THE RELATION OF THE TEMPORAL MUSCLES TO THE VENOM.
a, *a*, Anterior temporal muscle; *b*, its insertion in the lower jaw; *c*, venom gland; *d*, the fang half-erected (S. Weir Mitchell).

the venomized blood, the powerful local effect of the venom in inducing rapid necrotic changes in living tissues, and its action upon the wall of the capillary blood-vessels, which, failing to resist the normal blood-pressure, allows the corpuscles to escape into the tissues. The respiratory centers were shown to be profoundly depressed, and this, together with the cardiac paralysis, hemorrhages into the medulla, and the disorganization of the red corpuscles, was considered to be the cause of death. They concluded that venoms contained two or more proteids, a globulin, and a peptone, and considered these as the toxic elements, each having a separate effect upon the tissues of the organism. Mitchell and Reichert also foreshadowed antitoxin by clearly stating that the search for a chemical antidote would prove well-nigh hopeless, and that a physiologic antagonist must be provided, although the complexity of the venom made even this attainment difficult. Lamb [9] nearly twenty years later concluded that from experimental and clinical observation of the sera prepared by Calmette and by the Pasteur Institute of India the specificity of different venoms and the enormous dosages required militated against any practical application of antitoxin treatment.

Wolfenden [10] in 1886 made a careful chemical study of venoms obtainable, and concluded that the "peptone" of Mitchell and Reichert is probably an albumin. He also showed that the toxicity of venom is not due to any bacillus, bacterium, or living organism, nor to a ptomain or alkaloid, a view especially upheld by Gautier.[11] The exact position of the various constituents of venom in the proteid family, however, remains unsettled, the constituents of various venoms giving atypical reactions, and the conceptions of different investigators differing.

During the past ten years an enormous amount of work has been done upon the physiologic chemistry of snake venom, its toxicity, and especially its relation to immunity and immunization, much of which as yet has not been applicable to practical medicine. In 1895 Calmette [12] and almost simultaneously Fraser [13] prepared an antivenene, and prompted an almost endless chain of investigation and controversy among other workers. The differences apparently proceed from the complexity of the venom of different snakes, for it has been found by Flexner and Noguchi [14] that cobra venom owes its toxicity chiefly to neurotoxin, rattlesnake (crotalus) venom mainly to hemorrhagin; and therefore a serum prepared from the cobra fails entirely to protect against rattlesnake venom because of its absence of power against hemorrhagin.

The difference in the toxicity of various venoms has long been known, and depends not only upon the variety of snake but upon the amount of venom expelled, the latter fact, impossible to elicit in a given case, having the greatest possible influence upon the prognosis. Mitchell and Reichert regarded the order of toxicity of the snakes upon which they experimented as cobra, copperhead, water moccasin, and rattlesnake; Flexner and Noguchi arrived at practically the same conclusion. Fraser [15] states that the toxicity of the venom of the cobra is about 16 times greater than that of the rattlesnake.

Briefly, snake venoms have been divided into two broad classes: the colubrines, of which the cobra, king cobra, and krait are types; and the vipers, in which the rattlesnake and Russell's viper of India (*Daboia Russellii*) are included. The former, or colubrines, produce a paralysis of the respiratory center in the medulla and the motor end-plates of the phrenic nerves, affect hemolysis variously, reduce the coagulability of the blood, and do not produce extensive hemorrhagic effusions. The venom of the cobra has a much greater hemolytic action than the other colubrine venoms, but in all of them the neurotoxin is probably the potent factor in producing death.

The viper species differ somewhat in their production of thrombosis within the vessels, Russell's viper producing marked thrombosis, while in rattlesnake poisoning there is a marked absence of intravascular clotting. This difference, however, is said to be one of degree only, and due to a difference in the amount of the thrombosis-producing element in the different venoms and to the amount of venom injected. The rattlesnake venom has a much less hemolytic power than the cobra venom.

Pathology.—But little is actually known of the morbid anatomy of the tissues after death from snakebite because of the few autopsies that have been made, and because when death takes place instantaneously there is little reaction except the local one. In *cobra* poisoning the subcutaneous tissue at the point of injection is edematous from bloody serum and the neighboring tissues are congested. The blood is fluid and dark red in color, the body in a state of rigor mortis, the internal organs, especially the lungs, are hyperemic, and the veins of the pia are distended. The bronchi may be filled with frothy mucus and the mucous membrane congested.

After *rattlesnake* bite the tissues about the point of injection are markedly infiltrated with bloody serum and fluid blood, even the muscles being involved, not only near the wound but at a distance; sometimes they are disintegrated. The peritoneum, especially the mesentery, the pericardium, endocardium, rarely the pleuræ, and the mucous membranes, are the seat of blotchy patches of ecchymosis. The organs, especially the pelvis and glomeruli of the kidneys, are hemorrhagic. The peculiar hemorrhagic character of the lesion in *crotalus* poisoning has been explained by Flexner and Noguchi by the cytolytic effect of the toxic constituent contained in rattlesnake venom—hemorrhagin—upon the endothelial cells of blood-vessels. The extravasations of blood take place not by diapedesis, but through actual rents in the vessel walls. The latter appear as though solution of the wall has occurred at some of the points of contact with the venom, the adjacent endothelial cells appearing forcibly displaced outward by the force of the escaping blood. They also note that the condition of stasis in the vessels is accompanied by disappearance of the cell contours and not by agglutinations of corpuscles. Their studies also suggest that the softening of the tissues which favors the hemorrhagic extravasations may be caused by venom enzymes. The rapid occurrence of putrefactive changes in these degenerated tissues has been shown by Welch and Ewing [16] to be due to the loss of the germicidal property of the blood plasma, and Flexner and Noguchi proved that this phenomenon results from the union of the bactericidal complements with venom amboceptors.

Symptomatology.—As will be understood from the foregoing remarks the symptoms following snake bite are varied and diverse, depending on the variety of snake, the amount of venom injected, the resistance of the individual bitten, and the method of introduction of the venom, subcutaneous or into a vessel. The latter accident need hardly be considered, as death occurs almost instantaneously from general thrombosis, and the patient vomits, collapses, and dies without time for local symptoms to take place.

Cobra Bite.—Following the bite a burning pain is experienced with local redness, tenderness, and a gradually extending edema. Within an hour the constitutional symptoms appear, the patient, who has been very apprehensive, becoming drowsy, faint, and weak in the legs, staggering at first and later being unable to stand. There is ptosis, profuse salivation, dropping of the lower jaw and paralysis of the muscles of the tongue and larynx, inability to speak or to swallow, nausea and vomiting, but consciousness is retained. The paralysis soon becomes general, the patient lies prone and motionless, and the respirations, which were, at first, quickened, become slow, labored, and shallow, and finally cease. The pulse, also, at first, accelerated, becomes feeble synchronously with the respirations, but beats with moderate strength for a few moments after breathing ceases. Slight convulsions then occur, probably from asphyxia, the heart stops beating, and death has occurred in from three to fifteen hours; in favorable cases the patient quickly recovers without after-effects.

Rattlesnake Bite.—Following the bite the local symptoms are pronounced; the wound is the seat of marked pain and is surrounded by great discoloration from the extravasated blood. Hemorrhages may occur from all the mucous membranes and the conjunctiva becomes suffused with blood. Constitutional symptoms may develop in fifteen minutes, but usually occur in a few hours and are characterized by increasing prostration, nausea, vomiting, and a rapid feeble pulse with lowered blood-pressure. The respiration becomes slow and stertorous from paralysis of the pharyngeal muscles, convulsions are followed by paraplegia of the lower extremities, which, ascending, may cause complete paralysis, in which stage the patient may die within twelve hours after receiving the bite. If death does not occur the local symptoms become prominent, multiple hemorrhages taking place in the tissues, the swelling and discoloration rapidly spread, and the patient may succumb after the lapse of some days from sepsis. If recovery takes place it is usually very sudden, although the tissues often break down, leaving ugly suppurating wounds, sometimes even with necrosis of the bones.

Prognosis.—The prognosis depends upon the many factors previously mentioned, wounds upon the extremities being more favorable than those of the face or chest. In America, Mitchell gives the mortality as varying from 12 to 25 per cent., and Ellzey[17] claims it is 15 per cent. In Europe Bollinger[18] gives 10 per cent. as the mortality, Fayrer[19] in India places it at from 25 to 35 per cent., and in Australia it is said to be 7 per cent.

Treatment.—A countless list of remedies has been suggested for the cure of persons bitten by poisonous snakes, which, up to a comparatively recent period, have been based upon unscientific and even superstitious reasoning. Scientific treatment depends upon the neutralization of the venom at the point of inoculation, prevention of its absorption, the relief of the constitutional effect of the virus, and the rapid elimination of the poison. It would serve no useful purpose to recount the many remedies advocated. The following plan of treatment is based upon the views of recent writers whose experience in treating the condition has warranted the methods advocated. At any time a new plan of treatment may be urged, especially if an antitoxin can be prepared to neutralize all varieties of venom.

Local Treatment.—An elastic ligature should immediately be placed above the seat of the bite to prevent absorption of the venom, several ligatures being even better than one. This practice is a very old one, and perhaps the only one that has survived the test of time. Immediately following the application of the ligature a large area about the point of inoculation should be excised and the tissues injected in several places about the bite and at no great distance from it with from 20 to 30 c.c. of a fresh 1 per cent. solution of chlorid of calcium or chlorid of gold. The part should then be washed with a large quantity of a sodium hypochlorite or calcium chlorid solution, and as soon as possible the patient should receive by subcutaneous injection 20,000 units of antivenene. This method is practically that of Calmette.[12] In the absence of the above chemicals, pure crystals of potassium permanganate should be rubbed into the wound after incising or excising the bitten area, as recommended by Fayrer, Brunton and Rogers,[20] and others. A number of recoveries have been reported after the use of the permanganate crystals. A frequently recommended custom is the sucking of the wound to extract the poison forcibly, and though of doubtful value this may be tried until a knife is obtained to open the tissues freely.

General Treatment.—Strychnin, ammonia, and alcohol are the best stimulants of the many which have been advocated. *Strychnin* has been mostly vaunted by Mueller [21] in 1889 and Huxtable [22] in 1892, who claimed almost infallible results by its use. It is a powerful stimulant and may save life in cases where the minimal lethal dose of the venom has been injected, but is only an adjuvant to the local treatment. Alcohol and ammonia also act through their stimulating effect, have no specific action, and the use of massive doses of the former should be discontinued.

Artificial respiration, as suggested by Mitchell, is valuable because on theoretic grounds the heart-beats cease after respiration stops, and practically because Fayrer and Brunton insist on its use from the good results which they have obtained. The method should be persisted in for some time, always remembering that sudden changes are the rule in venom poisoning.

Lavage of the stomach may be of service by relieving the stomach of part of the poison excreted into that organ, and diuresis and diaphoresis have been recommended, but are of doubtful utility.

Antivenene, injected subcutaneously, offers the best and most promising method of neutralizing the poison *in vivo*. Calmette's serum or antivenene has been found to be of the greatest efficacy in the treatment of the colubrines, exerting a decided neutralizing effect upon the cobra venom, but it is not antihemorrhagic, the hemorrhagin being destroyed by the heat employed in its preparation. Consequently it is of doubtful utility as a curative agent against the venom of the rattlesnake. As yet no reliable antitoxin has been prepared for the venom of the latter serpent, because if the destructive local effects of the venom are removed its antidotal properties are also destroyed. Flexner and Noguchi recently have attempted to prepare such an antitoxin by transforming the locally active principles of crotalus venom into toxoid modifications.

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CHAPTER XV.

THE TRAUMATIC FEVERS.

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Confusion in surgical nomenclature is nowhere more productive of misunderstanding than in the discussion of the traumatic fevers. In current text-books and medical literature many of the following terms are used synonymously, or with vague idea of differentiation: traumatic fever, surgical fever, toxemia, septicemia, suppurative fever, sapremia, septic fever, infection fever, sepsis, putrid or septic intoxication, blood-poisoning, pyemia, septicopyemia, and some others. Most of these terms are unnecessary and should be discarded. Those we retain should mean a definite clinical entity to prevent misunderstanding and disagreement among medical men, and the mental picture to be portrayed should be kept clearly in mind by medical writers and speakers.

The classification offered in this chapter furnishes a simpler and it is hoped a more satisfactory nomenclature than heretofore for the traumatic fevers.

Terms such as traumatic fever, suppurative fever, surgical fever, infection fever, septic fever, septic and putrid intoxication, and septicopyemia, are compound terms. They are ambiguous and should be discarded.

Blood-poisoning is a term indiscriminatingly used by the laity. It may be used by medical men at the bedside for the benefit of the laity to cover either form of traumatic septic fever. It is not permissible as a scientific term.

Intoxication as a term should be limited to apply to the early stages of alcoholic poisoning, and the emotional stages of general anesthesia.

Surgical scarlet fever is described by some writers as a fever following traumatism and characterized by a rash like that of scarlet fever. Toxic products not of parasitic origin, and parasitic poisons, especially those of streptococcic origin, when present in the blood at times produce this rash. It is properly described as a scarlatiniform rash, and is to be classed with the erythemas, usually erythema multiforme, or with urticaria. Differential diagnosis between scarlatina and scarlatiniform rash is at times difficult, especially in the early days of a traumatic infection. Leukocytosis is common to pyogenic infection and scarlet fever and may be present in urticaria and erythema. Eosinophilia is present in scarlet fever and may be present in urticaria and erythema, but in the two latter diseases eosinophilia is not so constant nor so high in degree as in scarlet fever. If continuous fever, angina, enlarged submaxillary and cervical glands, nephritis, leukocytosis, eosinophilia, and later desquamation are present, the case is scarlet fever. If involvement of the throat and glands and the hemic conditions mentioned are not present in the first few days after a traumatic infection, a rash such as has been described is scarlatiniform, but the infection is not scarlet fever, and should not be so called. When we learn to isolate the organism causing scarlet fever, diagnosis in these doubtful cases will be readily made by positive or negative finding. Mallory asserts that Cyclasterion scarlatinale, a protozoön, is the cause of scarlet fever.

The term malarial fever is at times applied to obscure cases of septicemia, especially when the use of quinin seems beneficial in controlling chills and sweats. Accurately used, the term is permissible only when the plasmodium of malaria can be found in the blood. If it exists as a complication of a septicemia it is to be treated as a secondary infection, which fortunately for the patient yields to internal treatment by quinin.

Sapremia is widely used as a term for a form of septicemia, and is variously defined by authors. Park defines it best as "intoxication produced by absorption of the results of putrefaction of a contained material within a more or less shut containing cavity." He says, further, "So soon as the process spreads from the containing tissues the case merges from one of sapremia into one of septicemia." Theoretically Park's construction of sapremia may hold, but practically and clinically it is open to several criticisms. If it is accepted, pathogenic bacteria should be included as agents acting as do the saprophytic bacteria in a cavity. The definition is too theroretic in that only microscopic examination of the neighboring tissues could eliminate the presence of bacteria, which bacteria under favorable circumstances are disposed of by phagocytosis and the bactericidal property of the blood, especially when wise surgical measures are used in the treatment of the case. Lastly, the disease in its clinical features closely resembles septicemia of mild type, and its treatment is the same. If such a case promptly recovers it was possibly a sapremia, and if it does not it is positively a septicemia.

DaCosta agrees essentially with Park, but lays especial stress on the absence of infective property in the blood of sapremic patients, due to the absence of bacteria. Hence he would need to class diphtheria as a sapremia, the bacteria not being found in the blood. Tetanus would need a class by itself, the tetanus bacillus not being found in the blood, and the toxins being capable of producing the disease when injected into the circulation.

From another point of view the term sapremia, meaning "rotten blood," may be discarded. Its derivation and meaning are not helpful or logical. Septicemia, literally not much better in meaning, is generally accepted by medical men to mean a parasite or a parasitic poison in the blood, and is a term broad enough to include all septic conditions, whether of toxin absorption or bacterial invasion of tissues. It only needs differentiation medically from toxemias and surgically from aseptic fever, on the one hand, and pyemia on the other. Pyemia, meaning pus in the blood, in its turn does not picture the condition it is intended to describe, but it has been so generally used for years to cover certain clinical conditions and manifestations that it would be most unwise now to seek another term.

Toxemia is a term to retain in medical and surgical nomenclature. It must, however, be differentiated from a septicemia. From their derivation both words point to toxic products or poisons in the blood, and both are used by clinicians in this sense. The internist more frequently uses the word toxemia, the surgeon septicemia. Theoretically, toxemia should apply to the diseases in which one or more poisons are present in the blood which are not of parasitic production, while septicemia should be applied to diseases which present poisons in the blood that are of parasitic origin, the parasite itself being present or not present in the blood. The word poisons is here used in a broad sense to cover any substance applied to the body, ingested, or developed within the body which causes disease. It, of course, includes ptomains, leukomains, toxins, and sepsins. Toxemia, according to this definition, would include the diseases due to poisons not arising from parasitic invasion of the tissues and fluids of the body, at times of vegetable and alkaloidal nature, such as muscarin, strychnin or morphin, or an acid such as toxicodendric acid; again, of animal origin, such as the toxin of snake venom, the ptomain tyrotoxicon of milk or the ptomains of shell-fish; then again a mineral, such as arsenic or lead; and, lastly, the poisons of leukomain nature arising from disturbed excretion and perverted metabolism, and grouped under such terms as cholemic, intestinal, or uremic poisoning. Septicemia, in strong contrast according to the definition, would include diseases arising from invasion of the tissues and fluids of the body by animal or vegetable parasites, or their poisonous products. These poisons would admit of classification under a general heading, such as sepsins, whether ptomains, leukomains, or toxins. The invasion just described is termed an infection. The poisoning is called a sepsis. The adjectives toxic and septic mean poisonous. The former should be applied to toxemias, the latter to septicemias.

Autoinfection is a term to discard. The word is wrongly used by some writers to cover toxic conditions developed within the body by metabolic processes, or due to perverted secretion or excretion on the part of intestine, liver, kidneys, lungs, or skin. These conditions should properly be called autotoxemias or autotoxicoses. Occasionally they are less correctly called autointoxications. When the term autoinfection is used for any form of parasitic invasion it is a misnomer. Such an invasion is an infection. If the individual unintentionally or deliberately infects himself elsewhere from a primary focus, as, for instance, from a chancroid, it is called an autoinoculation.

Unfortunately for definition and classification, common use sanctions a broader meaning of the term toxemia than the one just given and explained. It is made to include a large number of bacterial diseases usually classed as medical and treated by the internist, such as typhoid, grippe, tuberculosis, pneumonia, etc. In the same comprehensive and mistaken way the poisons of these diseases are called toxins, whether chemically they belong to the toxalbumins or not. The same common use cramps the broad application of the term septicemia, limiting it to include the diseases due to infection usually classed as surgical, whether the knife is or is not used in their treatment by the surgeon.

Such a classification is, of course, arbitrary. Its excuse is common use. Until our knowledge of the products of parasitic life, ptomains, leukomains, toxins, and sepsins, and the poisons produced by chemical changes in the body is more exact, each new attempt at classification is apt to add to the excess of terms now in use. It is wise to refrain from coining new terms, but it is not unwise to limit and define the terms we now have. We therefore speak of the toxemia of intestinal indigestion, of uremia, of cholemia, and of the germ diseases usually treated by the internist. We speak of the septicemia of such diseases as erysipelas, tetanus, anthrax, and all diseases due to pyogenic and other less frequent infections needing surgical treatment. In pulmonary tuberculosis the internist may be allowed to speak of tuberculous toxemia, while in tuberculosis of bone the surgeon consistently speaks of tuberculous septicemia, especially when a secondary infection or an original mixed infection makes the constitutional condition one of a pronounced septic type. The same observation holds true in other toxemias; for instance, typhoid. The surgical sequels due to the typhoid bacillus are grouped in Keen's classic work on the "Surgical Complications and Sequels of Typhoid Fever."

With the theoretic definition of toxemia and septicemia in mind it is plainly seen that the differential diagnosis between traumatic aseptic fever, which is a toxemia, and the traumatic septic fevers, which are septicemias, is of prime importance to the clinician in his effort to promote the welfare of the patient. Differential diagnosis between different types of traumatic septic fevers is not so important, especially when such differentiation hinges on distinctions which are largely theoretic and not capable of clinical demonstration. We may therefore wisely reduce the number of subdivisions of traumatic septic fevers to the minimum, thus eliminating confusing terms and gaining clearness in diagnosis and nomenclature.

The nature of fever is still a subject of research for physiologist and pathologist. It may be defined as an elevation of body-temperature above normal (37° C.—98.6° F.), which elevation is usually accompanied by constitutional disturbances of function. As to cause, fever may arise from purely nervous disturbance, as, for instance, after fright, due to irritation of the heat center. The same center is acted upon by many substances which may be experimentally injected into the circulation of animals, some inorganic, some organic, as, for instance, water, ammonia salts, pepsin, fibrin, and other ferments and blood-serum. Fever also promptly follows the injection into the blood of the products of parasitic life, especially of bacterial life of the pyogenic type.

The traumatic fevers are febrile conditions accompanied by definite symptom complexes which follow traumatisms anywhere to the body, whether infection of the contused or wounded area does or does not occur.

Following traumatisms the traumatic fevers develop within a few hours, or they may not develop for several days, or still later after weeks or months, as sequels due to infection of the tissues which were lowered in their resistance by the traumatism.

The *traumatic fevers* can be simply and rationally divided into two kinds: the *aseptic* and the *septic*. Theoretically and clinically the septic type admits of ready subdivision into two forms—*septicemia* and *pyemia*.

From the prognostic point of view some authors call the aseptic type of traumatic fever benign, and in contrast the septic forms are classed as malignant. Neither term is exact. The term benign is more properly used, as the prognosis of aseptic traumatic fever is good. The majority of cases of septic traumatic fever are not at all malignant, yielding readily to modern surgical treatment, especially if promptly and properly instituted. Septic cases always have serious possibilities, but the term malignant should be applied only to pyemia in which the prognosis is almost invariably bad. In the olden days of surgery before asepsis and antisepsis were understood there was reason for the term malignant in classing septic cases.

The traumatisms which cause traumatic fever include contusions, wounds, burns (including electrical burns) and scalds, sprains, fractures, and the injuries produced by chemical irritants. The traumatism may be accidental or intentional, due to criminal violence, or the result of mechanical or operative procedure by the dentist, specialist, internist, or surgeon.

Traumatic aseptic fever is the rule after closed contused wounds, clean incised wounds, the wounds of aseptic operations, sprains, and simple fractures. Septic fever more commonly follows open, lacerated, and gunshot wounds, burns and scalds, compound fractures, the wounds of operations in infected tissues, and wounds of operation with faulty technic of asepsis and antisepsis.

TRAUMATIC ASEPTIC FEVER.

Synonyms.—Benign Aseptic Fever; Surgical Fever; Aseptic or Primary Wound Fever; Traumatic Toxemia.

Traumatic aseptic fever is a toxemia which follows the traumatisms already mentioned when infection does not occur. It is due to the absorption of nucleins and albumoses in the effused blood. Other factors play a part, no doubt, such as the action of antiseptics on the blood and tissues, fibrin and other metabolic ferments, buried catgut and the reflex disturbance of trophic nerves, vasomotor and heat centers. Traumatic aseptic fever has no morbid anatomy. Locally hyperemia occurs after any of the traumatisms mentioned, be it a simple incised wound, a wound of operation, a burn, a fracture, or the crushing of a limb. The healing process promptly begins in the injured tissues and proceeds more or less rapidly to recovery with more or less complete restoration of function in the injured part, according to the severity or character of the traumatism, the nature and extent of the tissues injured, and the success obtained by the surgical judgment and skill of the attending surgeon.

Symptoms.—Traumatic aseptic fever, or traumatic toxemia, is characterized by local and constitutional disturbances more or less pronounced and commensurate with the nature and location of the traumatism, the surroundings of the patient and his physical condition. Subjectively, complaint may be made of feverish flushing of face or body, chilly sensations or chill, headache, backache, thirst, loss of appetite, nausea, sleeplessness and smarting, burning, itching, or pain in the wounded area, in the wound itself, or referred to the terminal distributions of injured nerves. The chill of traumatic toxemia is of moderate severity and not constant. Frequently it is only general muscular tremor and is seen in neurasthenics. It is not accompanied by sudden rise in temperature nor profuse sweating. When a chill occurs after the first twenty-four hours, or the initial chill is followed by another, the onset of some intercurrent disease, such as pneumonia or the development of an infection, should be suspected.

Objectively and locally ecchymosis and the cardinal features of congestion are found more or less pronounced about superficial wounds according to the extent and depth of the injury. Deep wounds, contusions, sprains, and fractures present swelling and ecchymosis from extravasation of blood without redness or heat. Traumatism of viscera and tissues of the body cavities may present no local external signs. Neighboring lymph glands may be moderately enlarged in the line of the lymph-stream, but active lymphangitis and phlebitis are absent. If antiseptics such as iodoform, carbolic acid, or corrosive sublimate have been used on wounds as dusting powders, in ointments, or in wet dressings, a drug dermatitis excited thereby may simulate an inflammation of microbic origin. Erythema traumatica is frequent after contusions, abrasions, the friction of bandages, or the pressure of splint or dressing. When such erythema is of long duration, dermatitis traumatica with thickening of the skin due to tissue production and later pigmentation may result.

Objective general signs of traumatic toxemia include fever, disturbed pulse and respiration, skin eruptions, mental unrest, dysuria, and constipation.

Fever.—The fever is usually ephemeral, lasting two or three days, occasionally four or five days, and infrequently longer. The temperature rises after the traumatism within twenty-four hours, describing a symmetric curve of moderate height, ranging from 99° F. to 100° F. in the evening. The height of the fever is reached usually on the second or third evening, and thereafter it gradually subsides within the next twenty-four hours or two or three days (Fig. 144).

After severe contusions and simple comminuted fractures or other injuries with much subcutaneous hemorrhage, fever may run as high as 102° F. or 103° F. for several days, and then diminishing continue for some days, or perhaps a week or two, the evening temperature reaching 99° F. or as high as 101° F. Subcutaneous and deep hematomata, gluteal or pelvic, for instance, also cause prolonged aseptic fever. Hemorrhages into serous cavities do the same, notably hemothorax, the temperature reaching 103° F. or 104° F. when absorption is most active in the first few days.

After minor injuries, and occasionally after quite serious ones, no fever is observed, the maximum elevation not exceeding 99° F., reaction being slight and the body functions not disturbed. This is especially observed after operations in which, although the dissection is extensive, preparation for operation has been thorough, hemostasis effectual, approximation of divided tissue planes accurate, and the minimum of foreign material left for absorption. Patients whose blood examination is normal or nearly so develop the minimum of toxemic disturbance after traumatism.

Pulse.—After rallying from the shock of traumatisms patients often have a normal pulse. With hemorrhage excluded, vasomotor disturbance will account for ephemeral tachycardia and abnormalities in pulse volume and tension. Besides traumatic toxemia, vasomotor disturbance may be due to one or more of the following excitants: anesthetics, anodynes, pain, fear, or other emotions. Acceleration of rate describes a curve in harmony with the temperature curve, but averaging markedly lower than is found with the same range of fever in septic forms of traumatic fever. Occasionally the pulse-rate is below the normal. When not an idiosyncrasy, it is due to recumbent posture and rest.

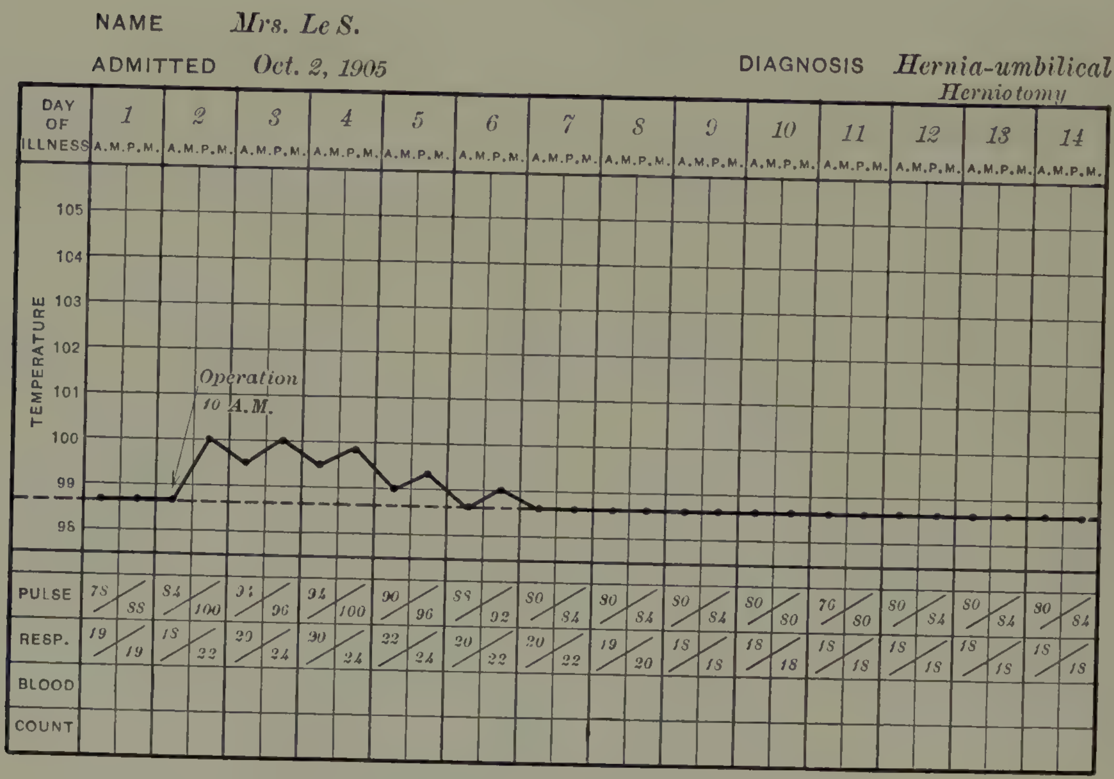

Fig. 144.—Chart of Traumatic Aseptic Fever.

Respiration.—The respiratory rate rises moderately, usually in keeping with the temperature. Occasionally it falls below the normal with subnormal pulse-rate already mentioned or under the influence of an anodyne. When marked increase of respiration is noted the cause may be bronchial irritation due to the anesthetic, fat or air embolism, or to beginning aspiration pneumonia or other intercurrent pulmonary trouble.

Following the shock of traumatisms neurotic and neurasthenic patients are prone to mental depression, emotional disturbance, irritability, and exaggeration of symptoms. Bedside notes may record sleeplessness, polyuria, hysterical paroxysms, or brief manias at times of suicidal or homicidal nature. (See the Chapter on Traumatic Neuroses and Traumatic Insanity.) Delirium, stupor, and comatose states are rarely seen in aseptic traumatic fever, except as a result of disturbed cerebral circulation after head-injuries or operations.

Anorexia is associated with the coated tongue of hepatic and intestinal torpidity. Constipation and scanty urinary secretion, due to lessened bodily exercise, reduced elimination, and inhibited excretion, are to be expected. Polyuria may be noticed when salt solution is used per rectum or subcutaneously to counteract shock. Phosphates and urates are frequently found in excess in the urine, but they have no serious significance. Albumin and casts may be found and are to be ascribed to previous renal disease or to active renal congestion, due to the anesthetic.

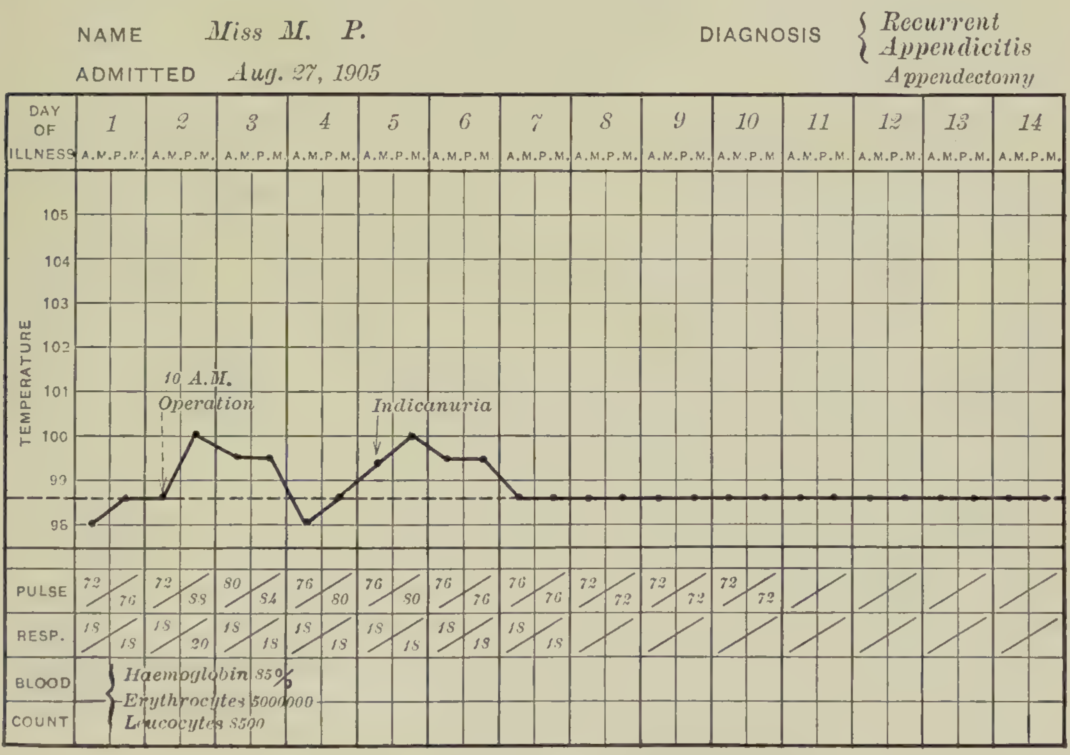

FIG. 145.—CHART OF TRAUMATIC ASEPTIC FEVER.

Occasionally after severe traumatisms the passive renal congestion of weakened general circulation causes temporary albuminuria with a few hyaline casts and blood-cells. When traumatism is done to the urinary tract itself, or catheterization is necessary, blood may also appear in the urine.

Angioneurotic edema occasionally occurs in neurotic patients. Local and general urticaria and erythema multiforme may occur and are generally due to the effect on peripheral nerves of the same toxic substances that cause fever. Occasionally they are entirely due to intestinal toxemia, and saline cathartics soon effect a cure. In the latter cases indicanuria may be found, and the stools often show imperfect digestion. The chart in Fig. 145 shows the course of the fever in a case of general urticaria occurring on the fourth day of traumatic fever after an interval appendectomy. Scarlet fever was suspected but soon excluded. The characteristic wheals of urticaria followed the finger drawn briskly over the skin. Calomel and salines were given. Free bowel movements followed, and the urticaria subsided gradually in the succeeding four or five days.

Examination of the blood reveals no especial change in traumatic toxemia. The anemia of hemorrhage or a moderate leukocytosis in the rally from shock and hemorrhage may be found in the early days of the healing process. This negative finding is of positive value in differential diagnosis between traumatic toxemia and traumatic septicemia.

Diagnosis.—The diagnosis of aseptic traumatic fever is based upon a history of traumatism (including in this term, of course, surgical operations), a moderate rise of temperature, usually within twenty-four hours, and the presence of some or many of the objective and subjective signs and symptoms just considered.

In doubtful cases dressings should be removed and the wound examined. Such an examination, if prematurely and needlessly made, exposes a normally healing wound to infection and shows the curiosity of timidity in the surgeon. On the other hand, to delay the removal of a dressing in the face of the signs of a beginning septicemia marks the over-confident or negligent surgeon. The traumatism of accidental violence demands removal of dressing when any doubt exists as to the nature of the resultant fever. Traumatism of planned and aseptic operation seldom requires such change. In both cases if the local features of sepsis hereinafter discussed are not found on change of dressing, and if intercurrent disease be excluded, the diagnosis of aseptic traumatic fever is fairly assured. If the run of fever and accompanying general signs persist, it may be necessary in the effort to arrive at a diagnosis to cut some of the sutures, reopening the edges of the wound where suturing has been done, or to make exploratory incision when hematoma or blood effusion into a serous cavity is present or is suspected. Exudates in serous cavities, like the pleura or the knee-joint, seemingly serous in character following traumatism, especially if by penetrating wounds, should be examined for bacteria. A smear properly stained may show microörganisms, and promptly classes such a case as a septicemia, thus avoiding delay in adequate draining, which a diagnosis of aseptic traumatic fever would entail. Bacteriologic cultures may also be made of doubtful exudates or from abraded surfaces, and especially from suspected mucous membranes, and diagnosis from negative results or positive growths may be obtained, although more slowly by several hours than by staining of smears.

In doubtful cases of traumatic toxemia a blood-count made at twelve or twenty-four hour intervals is most valuable. This is particularly so after internal injuries. A stationary white-cell count points to aseptic fever, though as high as 12,000 to 15,000, but a leukocytosis which rises in jumps of 1000 to 2000 between examinations is significant of infection, especially if associated with increasing percentage of polynuclear leukocytes and iodophilia.

Treatment.—The treatment of traumatic toxemia is expectant and conservative. Ordinarily enough anodyne to relieve pain, a saline cathartic on the morning of the second or third day of illness preceded by a hepatic stimulant the evening before if necessary, and restricted or fluid diet are sufficient measures to restore normal temperature and conditions within a few days or a week. Convalescence proceeds thereafter undisturbed by fever unless intestinal toxemia from constipation or some other complication should arise.

Requisite treatment is, of course, indicated for shock, hemorrhage, or other complicating disease or sequel of traumatism.

Nerve-sedatives and hypnotics may be needed for neurasthenic patients. Valerianate of ammonia, 5 to 10 c.c. (1½ to 2½ fldr.) every three or four hours; bromid of sodium, 1 to 2 gm. (15 to 30 gr.) every four or six hours; sulfonal or trional, 0.6 to 1 gm. (9 to 15 gr.) at bedtime, may be given for nervousness or sleeplessness. Larger doses of bromids must be given to alcoholics, particularly to habitual drinkers, to control restlessness and to avert delirium tremens. A generous dosage of whisky, approximating the daily habit, gradually reduced, is also advisable in these cases, especially after fractures.

Nausea and vomiting are more often the result of the anesthetic than of uncomplicated traumatic toxemia. Both may be relieved by the hydrated oxid of magnesia in 5 or 10 c.c. doses every two or three hours. It acts as a gastric sedative and a mild stimulant of intestinal peristalsis. Plain weak tea, a few drops of essence of peppermint in hot water, or cracked ice will often quiet nausea.

Backache is a result of disturbed renal circulation and muscle-strain sustained in struggling or while being lifted under the anesthetic. It is usually more severe when an anesthetic is used. Hot applications to the small of the back afford relief. When the urine is scanty and of high specific gravity water should be given frequently in small quantities by the mouth, or normal salt solution per rectum when vomiting is persistent. Thirst may be similarly controlled. Catheterization should not be done, unless distress from retention is felt, until eight to twelve or, when secretion is scanty at times, eighteen hours after injury or operation. Traumatic urethritis is difficult to avoid, although the greatest care is used in the procedure, and the catheter habit is developed and catheterization may be needed to relieve the patient for several days. Delay for twelve to eighteen hours except in traumatisms of the bladder is not harmful, and the patient, as a rule, regains vesical control in that time.

Neuralgic pains arising from traumatic neuritis or due to toxic products in the circulation must be controlled by hypnotics or anodynes. One to two grams of bromid of sodium may suffice, or 0.01 gm. of codein, 0.3 gm. of phenacetin, or 0.01 gm. to 0.015 gm. of morphin. To control pain morphin is the best remedy. Given in moderate doses hypodermically it not only relieves suffering, but quiets restlessness, checks nausea and vomiting, stimulates the heart, lowers the respiratory rate, lessens shock, and reduces reaction and fever.

The feeding of patients after injuries, and particularly feeding after operations, should be carefully regulated. Digestion is weak, secretions inhibited, and peristalsis slow. The habitual carelessness of the patient, and notably of his relatives and friends, in the matter of food leads to intestinal disturbance, complicating traumatic toxemia by adding an intestinal toxemia, thus lowering resistance and fostering a septic invasion which otherwise would not occur. Judicious starving of robust and healthy patients after traumatism or operation is conservative feeding. Soups and broths may be freely given to patients who have lost much blood. After injuries and operations involving the abdomen, and especially the stomach or intestine, feeding should be limited to water in small but increasing quantities by the mouth, or normal salt solution per rectum for two to four, and after some operations—as, for instance, an end-to-end anastomosis or a pylorectomy—even six days. Meat broths or white of egg should first be given, to be followed by milk and cereals, and later in the course of a week by more substantial food.

The immediate and late local treatment of the traumatisms causing aseptic traumatic fever is discussed under the headings of contusions, wounds, burns (including electrical burns) and scalds, sprains, fractures, and the injuries produced by chemical irritants, in the chapters devoted to those subjects. When sterile, dry, or moist dressings are used to cover wounds other than burns or scalds, the local reaction, as a rule, is simple hyperemia, or if extending some distance from the wound it is merely an erythema traumaticum. When solution of continuity has occurred, the reapplication of the sterile dry dressing or wet dressing of gauze moistened with sterile salt solution is best. Over this an ice-bag or hot-water bag may be used as indicated. Over unbroken, contused, ecchymosed, and painful areas the official cataplasm of kaolin may be used, or the hygroscopic effect of glycerin may be obtained by applications of pure glycerin. Extremities should be elevated to aid the return circulation, relieving excess of passive hyperemia. Hot-water bags and hot applications are also of benefit.

Prophylaxis.—From the prophylactic point of view, traumatic toxemia can be minimized by careful previous preparation of the patient before operations of election and the rigorous execution of all the details of modern aseptic and antiseptic regulations in operations of emergency. (See chapter on Operative Surgery.) Rest, quiet, pleasant surroundings and the hygienic details of ventilation, daily bathing, and suitable clothing are needed.

Prognosis.—The prognosis of aseptic traumatic fever is good. A serious prognosis does not arise except when some complication, such as shock, secondary hemorrhage, thrombosis, embolism, septicemia, or an intercurrent new disease, becomes the dangerous element in the case, under which circumstances the diagnosis and treatment have in view the complicating disease.

SEPTICEMIA.

Synonyms.—Septicemia; Secondary Wound Fever; Infection Fever; Suppurative Fever; Hectic Fever; Toxemia; Sapremia; Sepsis; Blood-poisoning.

Septicemia is a disease due to the presence in the tissues and fluids of the body of one or more parasitic poisons with or without the parasites. In this broad sense of the term the parasites may or may not invade the tissues, but the poisons produced by their vital activity, as well as the intracellular poisons within the parasites themselves, or the two kinds combined, can produce septicemia. A so-called catarrhal appendicitis or cholecystitis, due to colon bacillus activity, differs only in degree, as far as sepsis is concerned, from a general peritonitis, due to a pure infection of the same bacillus, the result of septic leakage into the peritoneal cavity after a perforation of the bowel by bullet or of appendix or gall-bladder by ulceration. It is not intended, of course, to overlook the toxemias due to perverted secretory and excretory functions of skin, liver, kidneys, intestines, and lungs, secondary to the presence of bacterial poisons in the blood and tissues. But such toxemias are not proper subjects for discussion in this chapter. With the early removal of their septic cause they usually disappear. If they persist as sequels after the sepsis is overcome, they are conditions calling for the internist, not the surgeon.

When the invading organism is within a body cavity, but not in the tissues or fluids of the body, a certain dosage of its elaborated poisons is absorbed. A more intense dosage of elaborated poison, to which must be added the intracellular poison, is absorbed when the parasites are favorably situated in the tissues or circulating fluids of the body. On this difference in degree numerous terms have crept into use, some of which have been discussed and discarded. When only the product of a pathogenic microörganism is present in the blood, as in diphtheria and tetanus, the term sapremia is used by some writers. A better way to distinguish these infections is to call them septicemias due to the specific toxins of diphtheria and tetanus. In a general way we speak of them as toxic forms of septicemia as opposed to the bacteremic forms in which bacteria are numerously found in the blood.

Emphasizing the nature of the poisoning, the toxins can be named when isolated and chemically classed. Assuming that tetanus toxin or combination of toxins producing the systemic effects of tetanus is called tetanin, it would produce tetanin septicemia, or, in other words, a tetanus septicemia. To speak of these diseases as toxic septicemias or septic intoxications is tautological, and unless the exciting organism is also mentioned is ambiguous, and when it is mentioned the combination is inelegant. A combination of the toxic and bacteremic forms of septicemia is seen in bubonic plague. In the majority of cases bubonic plague is due to plague bacillus infection of trifling wounds, and the bacillus travels to the nearest lymphatic chain. The resulting septicemia is due to the toxins, and hence is of the toxic form till the neighboring lymphatic chain protection is broken down, when the bacteremic form of the disease ensues, in which the bacillus is found not only in the first chain of glands, but generally in the blood. It is also of interest to note that in virulent cases of diphtheria, and chiefly in the fatal cases, the bacilli are found in the blood. It is also worthy of note that bacteremia is not always a septicemia. In fact, after the subsidence of a Bacillus mucosus capsulatus infection Duval and Lewis report a man as working and in good health who showed more of the bacteria in the blood existing in a commensal relation to their host than were found in the blood by cultures during his illness.

Cryptogenetic septicemia is a new term to cover our failure to find the point of entry of an infection. The old term was idiopathic or spontaneous septicemia. All of us are aware of trifling injuries—pin-pricks, bruises, or scratches—at the time of occurrence which we totally forget in a few hours or days. Exposed portions of the body and the interior mucous tracts also are punctured or abraded at times with so little of sensory nerve disturbance as to give no warning dart of pain. Theoretically these are the points of entry of the infecting agent in the so-called cryptogenetic form of septicemia. Urethral fever, so called, is an instance. It is characterized by chill and pyrexia a few hours after the passing of bougies or sounds and is ascribed by many writers to reflex nerve disturbance. It is due undoubtedly to traumatism of the urethral mucosa and transient infection. Occasionally it is followed, in fact, by a frank septicemia running the clinical course of an infecting organism, and rarely by pyemia.

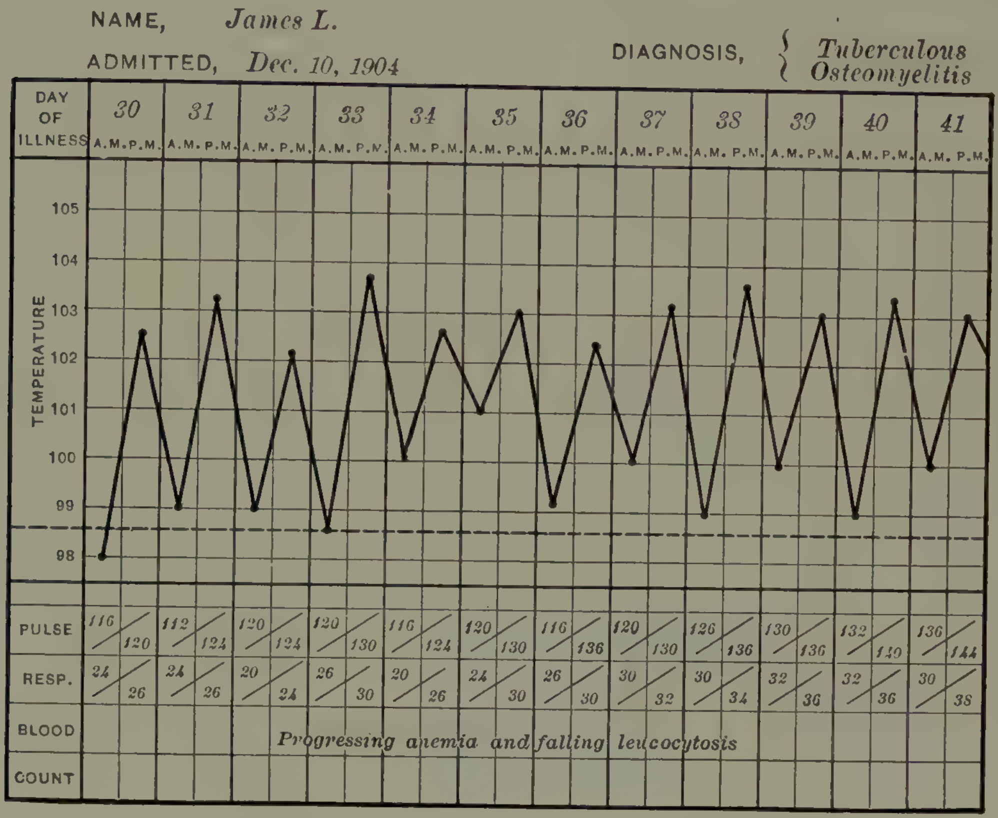

FIG. 146.—CHART OF HECTIC FEVER.

When a septicemia runs a long course, as it does in tuberculous and chronic suppurative conditions, with sudden rises and falls of temperature and accompanying chills and sweats, it is called hectic or habitual fever, especially by the older writers (Fig. 146).

Suppurative fever is described by some writers as accompanying abundant pus in abscesses. It, of course, is a septicemia, which is frequently due to the staphylococcus. When so, it would be better described as a staphylococcus fever, the tendency of this bacterium being to a circumscribed collection of pus, differing much from the streptococcus, which tends to spread more rapidly by the lymphatics, veins, and continuity of cellular tissues.

With the development of our bacteriologic knowledge a classification of septicemias will be advisable, based on the morphology and relationship of the infecting organisms and the nature of their poisonous products. Tetanus, glanders, typhoid, pneumonia, and other diseases have received specific names. We may, however, call them tetanus bacillus, bacillus mallei, typhoid bacillus, and pneumococcus septicemias, as we may speak of streptococcus, staphylococcus, and other pyogenic septicemias. Clinically they may be acute or chronic diseases, and from the prognostic view they may be mild, moderate, severe, or grave infections of the provoking organism, depending on susceptibility and virulence.

Septicemia follows the traumatisms already mentioned when infection does occur. The infecting organism may be implanted at the time the traumatism is sustained, being carried into the tissues by the septic agent inflicting the injury, or by a sterile agent like the surgeon's knife opening up a pathway to the deeper tissues for organisms present in the skin, or by spreading an infection previously localized by a wall of granulations, as in operating on an ulcer, sinus, fistula, or an abscess cavity. Again, aseptic wounds may become infected from unclean dressings or manipulation some time after traumatism, a traumatic septicemia supplanting a traumatic toxemia, or arising after the latter has subsided. Late infections may also be explained as due to parasites which gain entrance to the injured area from the blood- or lymph-stream, or if the injury occurs at the site of an old wound or of a previous and subsided infection, by the theory of a latent focus of infection, the organisms of a former active process being encapsulated and latent for years, to be started up afresh on the lighting up of the active hyperemia and lowering of tissue vitality resulting from injury. Occasionally healed wounds reopen with active pus formation and marked symptoms of septicemia, or healed wounds may undergo a process of cold abscess formation with low-grade septicemia, such wounds having previously healed with the signs and symptoms of aseptic fever.

When infection occurs after traumatisms a process ensues in which the system generally endeavors to overcome and destroy the invading organisms and to eliminate the toxic products of their life. In this process the phagocytic theory of Metchnikoff and the humoral theory of antitoxin or alexin formation play a part not yet fully understood. Locally there is added to the hyperemic process of repair the migration and diapedesis of cells and the exudates of inflammation. In the course of this process degenerative changes in the blood and tissues more or less rapidly develop according to the nature of the invading organism and the patient's resistance. In fatal cases slow in progress due to pyogenic organisms bacteremia is pronounced, the spleen and liver are soft and enlarged, and nephritis, gastro-enteritis and colitis, serous effusions, cutaneous and subcutaneous hemorrhages, and endocarditis are frequently present. In rapidly fatal types but little post-mortem change may be found macroscopically. Overwhelming toxic effect in these cases paralyzes circulatory, respiratory, and secretory centers. Parasites or their products or both may be demonstrable in the blood and tissues by the methods of the bacteriologist and chemist. Microscopically the cloudy swelling of early inflammatory degeneration may be found in the glandular organs, the brain and spinal cord, or generally in the tissues, and these changes are more marked if the septic process is protracted. The chronic or hectic fever form of septicemia seen in caries, necrosis, and tuberculous infections is sometimes followed by amylaceous or waxy degeneration of vessels and viscera. Clinically such cases are prone to develop edema, albuminuria with waxy casts, and the colliquative diarrhea of enterocolitis.

The parasites in the majority of all cases of traumatic septicemia are the pyogenic bacteria, most often the Streptococcus pyogenes and the Staphylococcus pyogenes aureus, less frequently the Staphylococcus pyogenes albus, gonococcus, Micrococcus tetragenus and pneumococcus, Bacillus pyocyaneus, B. coli communis, and occasionally the specific organisms of diphtheria, typhoid, tuberculosis, tetanus, anthrax, glanders, actinomycosis, and others.

Locally the clinical picture may range from a local blush to a phlegmonous cellulitis, or from a furuncle to a huge abscess. In deep infections, as in osteomyelitis or in the body cavities, the general features of a grave septicemia may seem out of proportion to the local signs of the inflammatory process hidden by the superficial tissues. Early operation by the correct diagnostician will reveal in these cases the fulminating character of the infection. The same infection attacked later, when the process has become unmasked by its progress toward the exterior of the body, results in extensive local inflammatory destruction and means a far more dubious prognosis for the patient.

Constitutionally the clinical picture may resemble a traumatic aseptic fever, or it may be distinctly different, yet benign from the prognostic point of view, or it may be from the first a prostrating disease, or, being mild at first, later become prostrating, serious in progress, and fatal in termination. All these possibilities depend on the nature and virulence of the infecting organism and the susceptibility and resistance of the patient. In tetanus local wound conditions may be septic in appearance if a mixed or pyogenic infection exists, but frequently the wound heals, as in aseptic traumatic fever, while the toxins of the tetanus bacillus produced from the spores in the course of ten days to two weeks cause the constitutional condition of fatal general convulsions. In anthrax a small painless vesicle, becoming in a few hours a pustule, marks the local invasion of the bacillus, but the constitutional condition rapidly becomes intensely septic with bacteremia, and if fatal with the post-mortem findings of destructive changes in the blood and glandular organ. Gonococcus bacteremia is associated often with endocarditis and monarticular or polyarticular synovitis and arthritis resembling pyemia. Streptococcus invasion of insignificant cuts and scratches often results in spreading destructive local cellulitis, teno-synovitis, periostitis or osteomyelitis, and general bacteremic septicemia, nephritis, gastro-enteritis, and other complications finally ending in death. Instances of infection due to other organisms might be multiplied, and a long argument to connect traumatism with the invasion of infecting organisms could be made. It is sufficient to refer the reader to the different chapters in this work to verify the frequency of infection and to prove the truth of the traumatic influences in septicemias.

Subjectively the patient usually complains of the same symptoms mentioned under traumatic toxemia, but his complaints are louder. Pain in and about the wound is more intense, and in the denser tissues throbs with the pulse, as in felons, owing to the extreme vaso-dilation of inflammation. Hot flushings with chills on slight draft or movement of the bed-clothing, and chills of pronounced type with chattering teeth and goose skin, occur. Chills may recur with more or less frequency, depending on the progress of the case, and are often succeeded by profuse perspiration or cold sweats, the temperature dropping several degrees. In place of chills, infants and adolescents are prone to have muscle tremors, or twitchings or general convulsions. Headache and backache are more severe, thirst is greater, nausea, vomiting, and anorexia are more marked, restlessness and sleeplessness are more pronounced, than in traumatic aseptic fever. Pressure and toxic forms of neuritis and accompanying neuralgias may excite bitter complaint from the patient. Weakness, emaciation, loss of muscle tone and volume, and exhaustion are daily more noticeable and alarming to the patient and his friends.

Objectively and locally in the early hours of the infectious process superficial wounds show the cardinal features of inflammation, with the reddish lines of lymphangitis, and the darker lines of phlebitis in the line of the lymphatic and venous streams. Neighboring lymph glands quickly enlarge, harden, become tender, and later may fluctuate when pus forms. Brawny induration of skin and subcutaneous tissue goes with septic dermatitis and cellulitis, and may end in purulent infiltration or abscess. Soft, boggy, and edematous skin may quickly develop overlying subcutaneous infections of virulent type, or after several days of inflammation in the less virulent forms. The tense, dull red blush with vesicating skin of erysipelas may appear. Pus foci may be seen in stitch holes and pus may well from between the edges of the wound. When putrefactive bacteria and the colon bacillus are present bad odor and gas may be noticed. In emphysematous gangrene and malignant edema gas may crepitate under the skin. This may also accompany septic processes due to penetrating wounds of the intestine or the lungs. Abscess, ulcer, sinuses, and fistulous tracts, areas of slough or extensive gangrene, serous, sero-purulent, and purulent discharge, pseudo-diphtheritic and diphtheritic membranes may be present. Over deep acute inflammations reflex muscular spasm leads to board-like rigidity of the muscular planes. If a joint is involved effusion into the joint cavity becomes apparent.

Muscular atrophy with contracture and flexion of movable joints associated with fixation of the joint results. The surgeon's pocket tape-line is needed to make exact record of apparent inflammatory enlargement combined with muscular atrophy.

Objective general signs of traumatic septicemia where they are the same as those of traumatic aseptic fever are more grave. In addition, certain alterations of the blood, of viscera, and of excretions, when found on examination of a patient are indicative of a septic process, and at times are distinctive of this process. When the anemia of hemorrhage or previous disease is not present, the flush of fever is noticeable in the patient's face in the early hours of a septicemia. Later anemia develops, the skin becomes less clear and sallow, acne simplex, herpes labialis, or furunculosis may develop, or an icteric tinge of hematogenous origin may be noticed. Later the face becomes anxious, the sunken eyes prominent and unnaturally bright, the features drawn and distressed. The tongue may be furred or dry and glazed. The breath becomes offensive. Sordes develops. Subsultus tendinum, involuntary picking at the bedclothes, fine and coarse muscular tremors, local hyperesthesias and anesthesias occur. Trophoneurotic impairment of the nerves and the dorsal decubitus often result in disagreeable and dangerous bedsores.

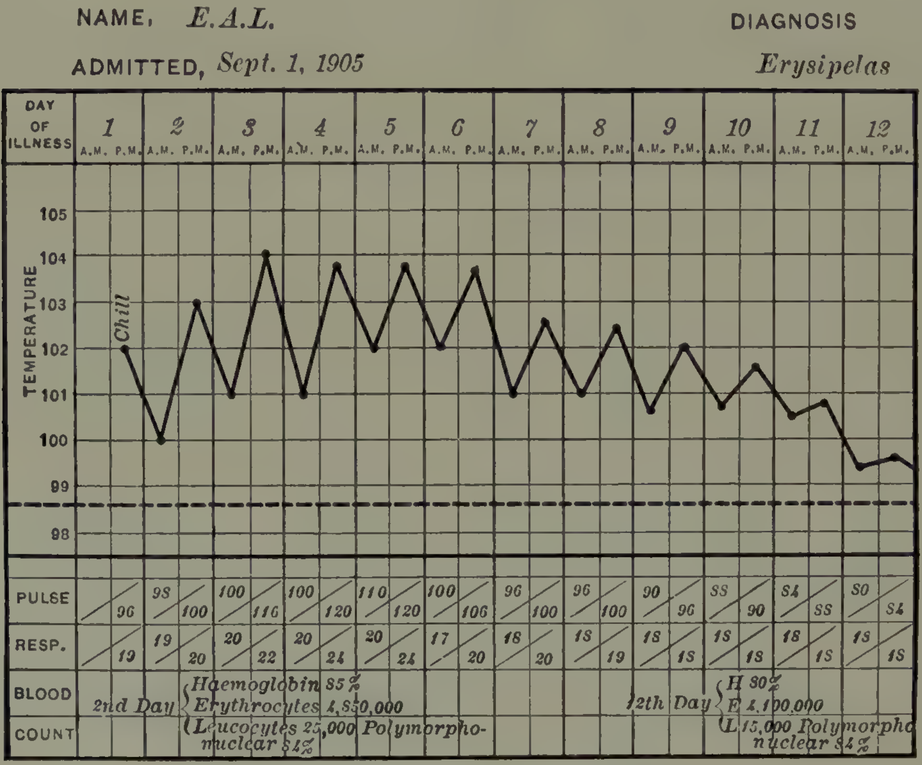

FIG. 147.—CHART OF SEPTICEMIA.

Fever may start as in traumatic toxemia and resemble it for two or three days, but continue thereafter instead of subsiding. In later infections after injury, of course, it starts later. It may show marked irregularity of rise and fall, and with extensions of the septic process may shoot up at any time in the day. As a rule, fever is high in the early evening hours and until midnight. From midnight till morning the temperature drops and may fall below normal, beginning to rise about nine or ten in the morning. Pyrexia, or fever, is called hyperpyrexia when the temperature is above 105° F. or 106° F. Hyperpyrexia is often followed by chill, sweat, and a sudden fall of several degrees. Subnormal temperature may be noted for days when prostration is pronounced or a low-grade infection is present. In these cases, however, at some time in the twenty-four hours a rise of temperature above normal will be recorded. (Fig. 147).

Upon evacuation of pus, establishment of better drainage by counter-opening, or removal of a septic foreign body, the temperature may suddenly drop and run normal or nearly so thereafter till the infection is overcome and recovery is complete (Fig. 148).

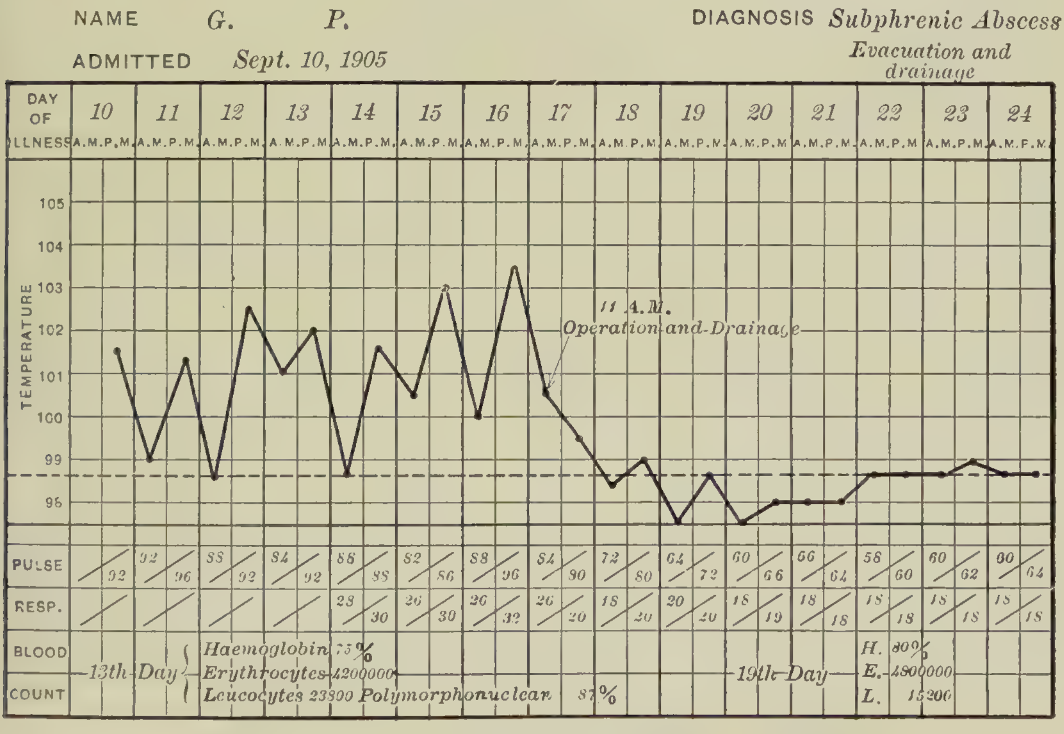

FIG. 148.—CHART OF SEPTICEMIA. DRAINAGE OF ABSCESS.

The strength and rate of the pulse are affected by the nature and dosage of the parasitic poison in addition to the influences which disturb the pulse in traumatic toxemia. It ranges higher from the onset of the infection even in mild septic cases. In more severe cases the pulse may reach 140 to 160 per minute within a few hours and be weak and thready, or rapidly fail till death occurs. As the pulse-rate ascends the temperature may rise correspondingly, or drop to subnormal, and so continue for a time in grave infections. Epistaxis, conjunctival ecchymosis, serous effusions and edemas may occur, due to alterations in the blood. The respiratory rate runs above normal in keeping with the pulse, and may average between 25 and 35 per minute in more serious infections, seemingly an effort at increased oxidation. Costal respiration is noticeable after abdominal injuries and with septic peritonitis.

The *mental disturbances* of aseptic traumatic fever are exaggerated in septic cases. Delirium is frequent, maniacal excitement, stupor, and coma are more often seen. Insomnia may be troublesome in the earlier days, and later be succeeded by drowsiness and the snoring sleep caused by the relaxation of the respiratory muscles. Depending on the nature of the infecting agent, the duration of the process, and the patient's susceptibility, the nervous system suffers locally and generally from the septicemias. The infections of rabies and tetanus confine their action to the nervous system and are terrifying in their deadliness, but no more so than an infection from a dissection wound which leads to the acute ascending paralysis described by Landry. Pyogenic organisms frequently excite septic meningitis in the cranial cavity or spinal cord, and their toxic effects produce various forms of neuritis, myelitis, and encephalitis during or following the septicemias. Spinal or cerebrospinal scleroses, disseminated scleroses, and degeneration psychoses and neuroses are some of the nervous sequels of infections.

Constipation is present in many cases of septicemia. In some acute cases and in many protracted cases enterocolitis develops, causing diarrheas. The stools may be serous or dysenteric, become more and more frequent, and finally incontinence may develop. Indican, blood, pus, albumoses, peptones, and more frequently albumin and casts, appear in the scanty urine. Bacteria may be numerous in acid urine, changing to alkaline bacteriuria with ammoniacal degeneration. Nephritis may cause suppression of urine and uremia may supervene, causing death. Retention and stillicidium or incontinence may occur.

The *cutaneous eruptions* of aseptic traumatic fever are more frequent in septic traumatic fever. So frequent is the scarlatiniform rash of urticaria multiforme that some writers speak of surgical scarlet fever, a term hereinbefore discussed and rejected. More characteristic of traumatic septicemia are the conditions of the skin due to deterioration of the blood in septic processes, purpura hemorrhagica, and subcutaneous hemorrhages. Secondary cutaneous infections around the wound, due to the streptococcus and staphylococcus, cause impetigo, ecthyma, furuncles, and carbuncle. Erysipelas may occur and is due to the streptococcus. The angioneurotic rashes of traumatic aseptic fever are also present, due to metabolic toxic products, such as ferments. Embolic action of bacteria stopping short of the pus production of pyemia causes the rose spots of typhoid in which the typhoid bacilli may be found. It is claimed that the protozoa of scarlatina and measles cause the distinctive eruptions in these diseases, and that the pustules of varicella and variola are due to protozoa.

Examinations of the blood, both bacteriologic and microscopic, are of especial value in the septic traumatic fevers. Recent improvement in technic makes such examinations especially helpful in the diagnosis of obscure septicemias, such as malignant endocarditis and streptococcus infections. Levy and Klemperer assert that bacteriologic examination of urine, sweat, and saliva should be made, as they contain the exciting organisms in septicemias. Bacteria in the blood are most readily demonstrable in pyogenic infections, in anthrax, and in gonorrhea. In many septicemias it is difficult to make cultures of the organisms in the blood until late in the disease, and then polyinfections of terminal nature may be present to make the diagnosis of the original infection obscure. Examination is made by withdrawing about 20 c.c. of blood from a vein under strict aseptic precautions and by culture methods determining the colonies of bacteria present. This is a laboratory method of the advanced medical schools and hospitals. Culture methods may also be applied to pus, serous and sero-purulent exudates, and pseudo-diphtheritic and diphtheritic membranes.

Cover-slip smears of blood are too uncertain for ordinary diagnostic work, except when the blood swarms with organisms. Smears of pus, sero-purulent and serous exudate, and from pseudo-diphtheritic and diphtheritic membranes are more certain to yield results. They may be made, stained, and examined in from two to five minutes, and in time to be serviceable in the treatment of a case during operation, as, for instance, in deciding the question of drainage. The technic for bacteriologic and microscopic examination of blood, pus, and exudates must be sought in works on bacteriology.

Microscopic examination of the blood depends on leukocytosis for its value in septic cases, especially on the increase of polynuclear neutrophiles. Accumulated clinical data point to the absence of leukocytosis in many diseases, such as tuberculosis and typhoid, and to its presence in the infections due to pyogenic bacteria, except under certain well-defined conditions, such as mild infections in strongly resisting patients, or loss of resisting power owing to overwhelming invasion, or gangrene with putrefactive rather than pyogenic organisms, or when the infection involves mucous surfaces or when exudation ceases. Leukocytosis is high when the infection is of virulent nature and the patient's resisting power is good. It may be high with a furuncle, and by reason of the exceptions just given it may be low in acute suppurative peritonitis.

Iodophilia or the reaction to iodin by the protoplasm of the neutrophilic leukocytes is also a microscopic aid to diagnosticating septicemias. Locke asserts that this reaction usually means septicemia, but not always pus. Cabot quotes Locke's conclusions in full. Iodophilia, however, is present in a number of toxemias.

It is safe to assert that leukocytosis and iodophilia are convincing and decisive factors in the diagnosis of septicemias, if taken as features in a clinical picture which includes many of the signs and symptoms just discussed. Taken with only a few of these clinical signs, it is wise to exercise a conservative prudence in deciding diagnosis on their evidence. Taken alone, they are unsafe guides in positive diagnosis of septicemia.

The methods of physical diagnosis are used to demonstrate suspected exudate in serous cavities, splenic and hepatic enlargement, endocarditis, and pulmonary complications. The sterile exploring needle on a glass-barreled hypodermic syringe is an invaluable aid to physical diagnosis in cases of suspected hydrothorax or pyothorax.

Diagnosis.—The diagnosis of traumatic septicemia is not difficult, as a rule. The nature of the invading organism, the point of entry, and the distribution of the infection are more difficult to determine, and yet are of paramount importance in prognosis and treatment. Immunizing methods of treatment are based upon a bacteriologic diagnosis. Anthrax, glanders, tetanus, diphtheria, and occasionally pyogenic infections are often masked in origin and progress till death is imminent. Streptococcus invasion, when it involves the skin, is plainly apparent, but the deeper manifestations of the bacterium in the female genital tract and elsewhere in the body after traumatism are sometimes productive of obscure septicemias. The diagnosis is based upon a history of the traumatism, a rise of temperature, usually ascending for two or three days and then continuing, and the presence of some or many of the signs and symptoms already discussed. Examination of the wound may reveal some of the evidences of infection enumerated. Positive findings by bacteriologic and microscopic examination of the blood and exudates are pathognomonic and are thus of more value than the negative findings by the same methods in aseptic traumatic fever.

Diagnosis is made more certain by exclusion of intercurrent and complicating diseases not traumatic in origin.

Prognosis in septicemia is always to be guarded, but it should be hopeful. The equations formed by virulence of infection, susceptibility, and resistance of patient, on the one hand, and mild, serious, grave, or fatal result on the other, are many and uncertain. Trivial injuries with insidious infections may result disastrously in local destruction or end in death, while most severe injuries with seemingly hopeless septicemia may be followed by recovery.

Bacteriologic and microscopic study of the infecting agent and of the blood, the careful study of the location of the infection and of the patient's physical condition, with the signs and symptoms of the disease, may make it possible to lean more positively one way or the other from a guarded prognosis, committing one's professional opinion to a favorable or a fatal termination of the disease.

Prophylaxis of septicemia demands the strict observance of precautions and methods of procedure mentioned under traumatic toxemia in regard to the preparation of the patient for operations of election and emergency and in the treatment of injuries. For the protection of others, especially in hospital practice, a judicious isolation of septicemic patients must be practised. A separate building, remote from the general wards of a hospital, should be provided for erysipelas, tetanus, diphtheria, and the exanthemata. Isolation wards should be provided for cases of septicemia and pyemia.

In the **local treatment** of septic wounds the principles of asepsis and antisepsis must be observed. Dressings of septic wounds should be done with gloved hands, primarily to make the hands altogether unlikely to carry the infecting agent to other patients, and secondarily for the protection of the surgeon or nurse. Infected dressings should be removed with sterile forceps and burned. No handling of pus-soaked materials should be done with the fingers, nor should the patient nor others run the risk of auto-inoculation or of communicating an infection to others.

Treatment.—The treatment of traumatic septicemia is both local and general. It aims to eliminate the infecting parasites and to neutralize their toxic products, to promote healing locally, and to uphold the system generally.

The point of attack on the infecting organism is the port of entry, if it can be determined. When it must be reached by inflicting the traumatism of an operation, the attack is made according to the principles of asepsis when dealing with clean tissues and wounds and of antisepsis in the treatment of infected wounds or of clean wounds positively or presumably exposed to infectious materials. This means antiseptic surgery for abrasions, burns, and scalds, the several varieties of wounds, ulcers, and gangrene, the incision and drainage of abscess, curetting or incision and drainage of sinus and fistulous tracts, the operative surgery of the bones, joints, and other systems and the viscera of the body, in short, operative surgery of different regions of the body when traumatism is suffered and infection occurs. To remove the cause of a septicemia may require minor or major operation; at times simple incision, at times mutilating operation, such as amputation, is called for in the effort to save life. To review the operative treatment of septicemias would be a repetition at length of that portion of the different chapters in this surgery dealing with the operative surgery of infections.

A general consideration of the subject is allowable in this chapter. Certain infections if suspected or demonstrated bacteriologically must be dealt with according to the nature of the organism before the septicemia matures. Local antisepsis for bites of rabid dogs is insufficient. Immunization by inoculation against hydrophobia is alone curative and life-saving. This is analogous to the treatment of the toxemia due to the bites of venomous serpents, which is most satisfactorily treated by antivenins. Protective injections of antitetanic serum are far more efficacious than the antitetanic serum treatment when the disease is fully developed. The same may be said of the antidiphtheritic serum treatment of diphtheria and of protective inoculation against the bubonic plague.

The antistreptococcic serum treatment of pyogenic septicemias is gaining in favor. The majority of surgeons can report some cases seemingly benefited by its use, especially in erysipelas. All surgeons who have used it have been disappointed in some cases. Favorable results are promptly reported. Negative results are less often recorded. The difficulty is to get a serum from a bacterium not only morphologically, but also in all other ways, the same as the infecting organism in the case to be treated. That some bacteria are not bacteriologic entities, but are forms of related groups, is probable. Levy and Klemperer assert that Bacterium coli communis is a collective term for several groups of related bacteria. Such a fact would explain the failure of some specific antitoxins. The antistreptococcic serums do no harm. Theoretically their use is indicated, and they should be used in serious septicemias refusing to yield to the accepted methods of treatment. Serum therapy is destined to be a boon to sufferers when perfected. In diphtheria, a typical septicemia of the toxic form, accumulated clinical evidence proves the success of the treatment by large and repeated doses of the antidiphtheritic serum; and the earlier the treatment is instituted, the better the results. Tetanus is also a septicemia due to toxins, but the antitoxin treatment is extremely disappointing. Bentz reports one favorable case in eight. Bacteriologic diagnosis of tetanus bacillus infection in wounds is practically impossible by our present methods, and later, after the clinical diagnosis is made and the toxin effect is fully developed, the antitoxin treatment is too late.

Locally the pyogenic infections are best treated by free drainage and the encouragement of the formation of a granulation wall to limit toxic absorption. Streptococcus infection needs more and longer incisions than does the staphylococcus invasion. Pyogenic infection of lymphatic glands usually causes acute abscess needing free incision. Tuberculous infection of lymphatics means extirpation and after-treatment with applications of iodin, while syphilitic infection usually clears up under mercurials and iodids without operation. Pyogenic infections of the extremities can be treated by Clinton's method. After meeting the operative indications he surrounds the area of infection by oilcloth and maintains a hot-air bath of 100° F., seeking to keep the tissues of the part at that temperature, and thus inhibiting bacterial growth. Bier applies the passive hyperemia treatment to low-grade infections by sufficient compression to retard the venous return circulation, thus securing the nutritive and bactericidal properties of the blood.

The **general treatment** of septicemia is nourishing, stimulating, and tonic. Full diet with eggs and milk between meals for low-grade and chronic infections is to be ordered, if well borne. Eggs, milk, butter and cream, nutritious soups and broths, cereals, and custard may be ordered for patients who have poor appetites and weak digestion. Egg and milk every four hours with soups occasionally may be given to patients more prostrated and disinclined to take food. Egg in water with whisky, or milk and whisky, may be all a patient will bear, or meat extracts, white of egg, and water. Occasionally rectal feeding by enemata of peptonized milk and egg must be resorted to for a time when the patient sinks into the so-called typhoidal state with sordes, delirium, vomiting, and prostration. Strychnin and whisky are the best stimulants. The former may be given in doses of 0.001 gm. to 0.002 gm. hypodermically every three or four hours, the latter in 5 c.c. to 15 c.c. doses every two hours. Antipyretics and all depressants are, as a rule, contraindicated. Iron is the best tonic. It aids the hydremic blood, increasing red cells and hemoglobin. No form of iron does as well in my experience as the tincture of the chlorid of iron in 1 c.c. to 2 c.c. doses before or after taking food. It promotes appetite, given before taking food, and aids digestion when given after meals. As a bitter tonic and an appetizer the elixir of iron and gentian in 10 c.c. doses acts well, or in place of strychnin the tincture of nux vomica can be given in 1 c.c. dose in water before meals. In chronic septicemias syrup of the hypophosphites in 5 or 10 c.c. doses, or Fowler's solution in 0.2 c.c. doses, after meals is beneficial. The alterative effect of arsenic is best obtained by increasing the dose one drop every third day till the beginning of limit of toleration is reached, usually eight to twelve minims; then decreasing in descending order as the dose is increased, and again increasing. In tuberculous septicemia cod-liver oil in 5 c.c. doses, or a larger dose of an emulsion, if the latter is better borne, and syrup of iodid of iron, 1 c.c. to 2 c.c. after meals, are indicated to secure the beneficial internal effect of iodin. Temporary administration of normal salt solution per rectum aids in elimination of septic products. In critical conditions of septicemia salt solution by hypodermoclysis, 250 to 500 c.c. under the superficial pectoral fascia on each side, alternating every four or six hours, may be employed. In desperate cases direct venous infusion of 500 to 1000 c.c. of salt solution is of value in stimulating inhibited excretion. The median basilic or median cephalic vein offers the best site for such infusion.

Tepid water sponging and alcohol rubs are the best antipyretics, acting also by stimulating peripheral circulation and developing a physiologic leukocytosis. Nervous disturbances and other conditions can be treated ordinarily with the remedies discussed in the treatment of such disorders under traumatic toxemia.

Discussion of special indications for treatment can be found in the proper chapters of this surgery, or, if outside the scope of a work on surgery, in the standard works on special subjects.

PYEMIA.

Synonyms.—Septico-metastasis; Suppurative Fever; Ichorrhemia; Thrombo-embolic fever; Blood-poisoning.

Pyemia is a septicemia characterized by one or more abscesses which may be disseminated from an original site of infection by infected emboli, or may be the result of an infection by the original infecting agent of distant thrombi due to toxic thrombophlebitis, thromboarteritis, or lymphangitis and lymphadenitis. Toxic materials in the blood may cause thromboses. If other organisms than the original infecting agent cause abscess development in such areas, the condition is one of secondary infection, also called terminal infection when occurring in the enfeebled patient in the final hours or days of his illness. Pyemia is in reality a metastasis or two or more metastases of an original sepsis in a patient. A more fitting name for this disease, from the points of view of derivation and meaning, is septicometastasis.

Pyemic abscesses are also called metastatic abscesses. They may be single or multiple, large or small. When they are small they are called miliary. The peptonizing or liquefying action of pyogenic microörganisms on blood-clot, particles of which are carried into the venous circulation, readily explains the formation of mestastatic abscesses due to broken-down thrombi of wounds. They are often found post mortem in the lungs, the first halting-place for emboli in the systemic veins. Infarcts of terminal arteriole areas involve the pleura, with resulting empyema. Small foci passing the pulmonary circulation and entering the arterial current are distributed elsewhere in the body, reaching the brain, liver, kidneys, and other regions, where septic infarctions and abscesses result. Emboli of parasites in sufficient mass to produce infarction in minute capillary districts also occur. Metastasis of pyemic nature from the portal system finds its first expression in mesenteric and hepatic abscesses.

Metastatic abscesses may also develop by way of the lymphatic system. After an infected wound of the finger or hand involvement of the axillary glands may occur with single abscess, several abscesses, or the matting of the group in one large inflammatory mass with several purulent foci. The lymph glands of the groin, axilla, and neck are frequently the sites of lymphatic septicometastases.

Thromboarteritis is more rarely a cause of pyemia. Denser arterial wall and arterial current resist thrombus formation. Emboli from such a thrombus travel only to the terminal capillary areas. Metastasis from ulcerative endocarditis is of this type.

Much has been written to explain cryptogenetic or spontaneous pyemia. Thrombophlebitis with abscess formation is known to occur at various spots in the body of bacteremic patients without post-mortem finding of emboli or site of original infection. Forgotten wounds, middle-ear disease, pyelitis, prostatic abscess, bronchial lymph gland, and other obscure infections are the original foci of infection in many of these cases and are often overlooked. Plain embolic cases of pyemia arising from wounds are described by some writers as extravascular, while cases of pyemia in which the course of the infection is not found are called intravascular infections. Acute ulcerative endocarditis is frequently a manifestation of the so-called intravascular pyemias. These terms are ambiguous.

Post-mortem findings in patients dying of pyemia are those of septicemia with more marked evidences of blood, visceral, and tissue degeneration, and in addition from one to many abscesses in various parts of the body.

Septicemic patients coming to post mortem with abscesses distant from the site of the original infection and due to other organisms are generally to be regarded as cases of septicemia with late secondary or so-called terminal infections rather than cases of pyemia.

The microörganisms of pyemia are mainly the pyogenic bacteria, the majority of cases being due to the streptococcus and staphylococcus. Other bacteria facultative in character as regards suppuration can produce pyemia. The synovitides of gonorrheal origin are mainly serous or seropurulent. If these cases of joint effusion were classed as abscesses, pyemia due to the gonococcus would be the most frequent form with which we have to deal. As it is, distinctly purulent forms of gonorrheal arthritis are fairly frequent. The clinical course of these cases ending in ankylosis or destruction of joints requiring resection or amputation, and at times terminating fatally, differs only in degree from other cases of pyemia. Typhoidal osteoperiostitis, arthritis, hepatic abscess, and other suppurative sequels are pyemic in character. The bacilli in pure culture have been repeatedly found in the pus from such cases. Pneumococcic arthritis of pyemic or metastatic type is also known. Acute miliary tuberculosis arising from penetration of a vein and distribution of tubercle bacilli by the blood-stream is of the same type. It is, of course, understood that many of the suppurative processes following the infections of gonorrhea, typhoid or tuberculosis, and other facultative bacteria are due to original mixed infection, or later secondary infection favored by the enfeebled state of health in the patient. It is fair to claim, however, that pyemic or metastatic forms of gonorrhea, typhoid, tuberculosis, and other pyogenic organisms arise, besides those of streptococcus and staphylococcus. Secondary or terminal infections may at times cause suppurative inflammations simulating pyemia, the original infecting microörganisms not having been disseminated, or at least not being found. Disappearance of one organism with the overgrowth of another is a known bacteriologic fact.

Clinically pyemia of the thrombophlebitic type is rarely seen now compared with the days of surgery twenty-five years ago. It is extremely rare after modern operations of election. It is most often seen nowadays in the emergency cases of the accident wards in septic cases coming for late operations, and in obstetric practice as a complication of puerperal septicemia, especially of septic metritis, owing to the ready distribution of infected emboli from softening thrombi in the uterine venous channels.

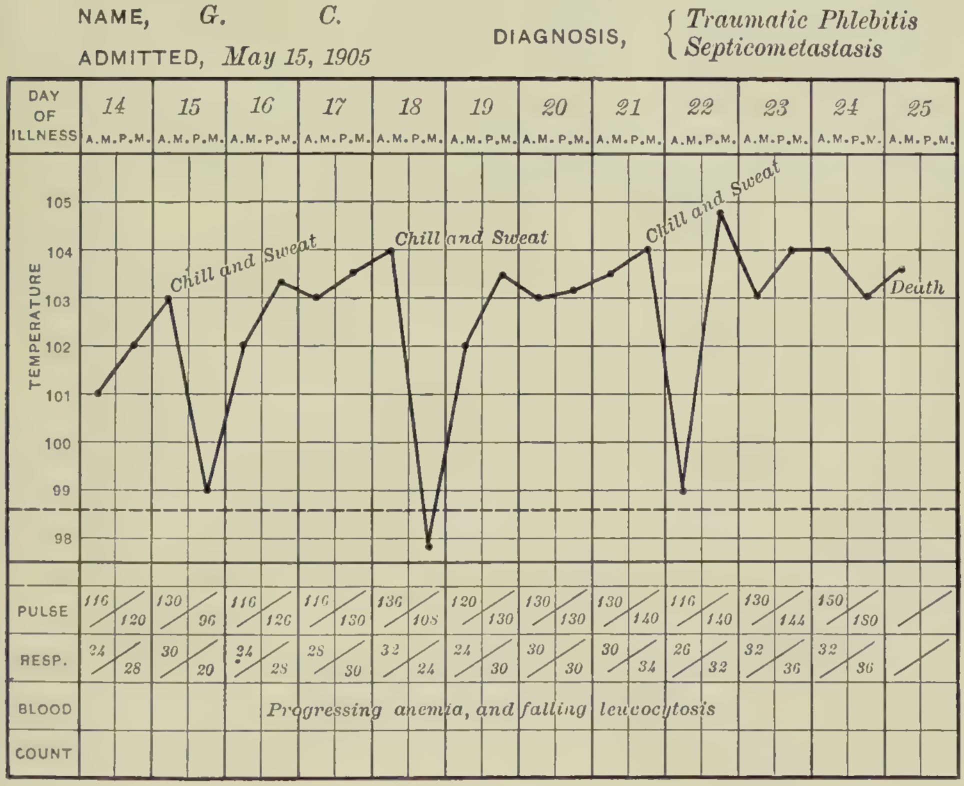

FIG. 149.—CHART OF PYEMIA.

Pyemia may develop several days after the healing of the wound of entry of the infection. Usually it develops in the first or second week of a plain septicemia of the pure pyogenic type or of the facultative pus-producing organisms.

The **symptoms** and **signs** of septicemia already discussed are naturally to be expected, and, as a rule, are intense in type. In addition in the locality of abscesses, the signs and symptoms of abscess are found. In large and superficial abscesses these clinical features may be evident and unmistakable. In small and in deep abscesses in the viscera and body cavities the clinical features may be quite obscure. Suspicion of abscess of metastatic type in a case of septicemia does not justify a diagnosis of pyemia with the consequent grave prognosis. It does justify all diagnostic measures to localize the suspected suppuration with a view to early treatment not only of the new purulent focus, but in the hope of attacking also the thrombotic focus at the site of embolus dissemination.

Pyemia is usually ushered in with a severe chill, often lasting several minutes, with temperature rising promptly to 103° F. or higher, becoming hyperpyrexia. Chills are severe and frequent, and are said to occur with each new abscess formation. One or several may occur daily, or they occur at irregular intervals of two or more days. Peripheral vasomotor relaxation and profuse sweat follows, and a temperature which has been 104° to 106° F. may fall several degrees, perhaps below normal. The interval between chills grows shorter as the disease progresses.

The fever of pyemia differs from that of septicemia. It is irregular, frequently missing the usual evening rise of septicemia and rising in the morning in place of the usual morning remission. It jumps several degrees before a chill or coincident with it, and falls sharply with and after the sweat. The strong contrasts of rise and fall are apparent on the temperature chart (Fig. 149).

Metastatic or secondary bronchopneumonia, pleurisy, synovitis and arthritis, meningitis and peritonitis, endocarditis, nephritis, hepatitis, and so on, occur and are to be diagnosed as in primary conditions of the same diseases.

Prognosis.—The prognosis of pyemia of thrombophlebitis and thromboarteritis due to pyogenic bacteria is bad, as a rule. Prognosis is more hopeful in pyemia due to other bacteria, especially when due to the gonococcus or the typhoid bacillus. The element of uncertainty is peculiarly present and disconcerting in pyemia because of the unknown number and location of embolic foci or metastatic thromboses. Chills, sweats, and exacerbations of fever seemingly overcome by incision and drainage of huge apparent abscesses soon recur, due to hidden internal collections of pus. Prostration and emaciation proceed rapidly in most cases. The breath is said at times to develop a sweet odor. The mind may remain clear, but stupor and a comatose state usually develop, and death occurs in from one to two weeks after the onset of purulent metastasis. The prognosis is better in pyemia due to lymphatic extension because of the barriers interposed by the protecting chains of glands. Abscesses can be readily attacked in superficial and deep lymphatic groups and spread of infection stopped. In pyemia due to thromboarteritis and embolism the prognosis, of course, depends on the location of the emboli, but the prognosis is theoretically better in a given number of cases than in the same number due to venous thrombus dissemination. When metastatic abscesses are superficial, affecting mainly the subcutaneous cellular tissue, or are confined to the joints of the extremities, the prognosis is improved by reason of the better possibilities of treatment.

Prophylaxis of pyemia is the same as that of septicemia.

Treatment.—The treatment of pyemia is that of septicemia plus the surgical pursuit of metastatic abscesses, which are to be incised, evacuated, and drained when accessible. It seems unjustifiable at times to attempt the operative treatment of unmistakable pus collections in seemingly moribund patients. While not unjustifiable, it is useless and unwise to operate if, in addition to operable abscesses, there are others beyond doubt inaccessible and inoperable. If the focus of infection can be reached and the thrombosed vein exposed radical extirpation of the infected thrombotic area should be practised to prevent further embolism. A thrombus of the lateral sinus due to middle-ear infection has been repeatedly cleared to normally bleeding vein and with a successful result. Gauze packing can be used to stop venous hemorrhage, or ligature of the vein above the excised area may be needed. The latter procedure is more readily practised in the extremities.

Secondary or terminal infections are complications which demand the local and general treatment laid down in other chapters of this work for such conditions of disease, modified by the requirements and limitations of the general state of the patient due to pyemia.

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CHAPTER XVI.

SCURVY.

By Charles Harrison Frazier, M.D.,

PHILADELPHIA.

Synonym.—Scorbutus.

Definition.—Scurvy is a constitutional disease, characterized by hemorrhage into the skin or subcutaneous tissues, gingivitis, anemia, and great debility.

Etiology.—Scurvy has been described in all ages and figures in many tales of travel and discovery, the ravages of the disease frequently decimating a crew during the long voyages in past centuries. Beginning with Hippocrates and Pliny, accurate descriptions have been written describing scurvy among the legions of Cæsar, the Crusaders of the middle ages, the cohorts of Napoleon, and even the forces engaged in the Civil War. In the Boer War a number of cases were reported, principally in the native Kaffir troops.

Scurvy may be epidemic, endemic, or sporadic, and may occur in any climate, country, or zone. No race is exempt; age and sex have some influence, most of the cases occurring in males and during middle adult life. While winter and spring witness the most cases, when in epidemic or endemic form no season is free from the disease. It may occur in the rich or in the poor, in hospitals, armies, jails, ships, or in a sporadic form in the home. Over-fatigue, impaired vitality, overcrowding, defective hygiene, and bad water are all predisposing causes. It may follow certain diseases, such as dysentery, typhoid fever, pneumonia, malaria, tuberculosis, rheumatism, etc., and has been reported as being transmitted from mother to fetus (Dohrn [1]). The theories of causation are three: (1) Nutritional, (2) toxic, (3) infectious. Each has its advocates, all have opponents. Since Bachstrom [2] in 1734 demonstrated that a lack of vegetables in the diet was the cause of scurvy, considerable attention and study have been directed toward ascertaining the reason therefor. Garrod[3] in 1848 concluded that "in all scorbutic diets potash exists in much smaller quantities than in those which are capable of maintaining health, and that all substances proved to act as antiscorbutics contain a large amount of potash." Garrod's ideas were not entirely corroborated by later observers. Bryson,[4] Grant,[5] Buzzard,[6] and others assumed the deficiency to be not the lack of potash salts, but the absence of the combination of potash with organic acids, such as citric, tartaric, malic, etc. Chalvet [7] in 1871 showed that the salts of the organic acids when injected with alkalies give rise to the formation of carbonates in the blood, and that the potash in meat and leguminous vegetables is not absorbed because it exists in some more stable form. In 1877 Ralfe[8] in a noteworthy and classic study placed the etiology for the time being on a sound basis by demonstrating experimentally that the disease is due to a diminished alkalinity of the blood produced by an increase of acid salts, chiefly urates, and by the withdrawal of salts having an alkaline reaction (chiefly alkaline carbonates); this diminution in the alkalinity of the blood finally producing the same results in scorbutic patients as happens in animals when attempts are made to reduce the alkalinity of the blood either by injecting acid into the blood or feeding with acid salts. Wright[9] claimed that scurvy is an acid intoxication due to the ingestion of an excess of mineral acids over the bases, and reported 7 cases in which the alkalinity of the blood was much reduced. Schmiedeberg and Walther[10] showed that man is able to bear up without injury against a moderate degree of acid intoxication, but if plied with acids beyond a certain point the alkalinity and coagulation of his blood will diminish and he will finally succumb to the acid intoxication. Wright points out the importance of this point in the deleterious effect produced by a diet of preserved meats and cereals, or of either of these separately, and he also explains the reason for the beneficial effect obtained by administration of blood or of fresh meat with the blood in it on the grounds that not only is the blood an alkaline food-stuff but that it is comparable in its yield of alkaline salts to lemon juice. Lamb[11] fails to agree with Wright and previous observers in certain of their statements. He observed eleven cases of scurvy in India, five of which occurred in prisoners in a jail near Bombay, where the quantity and quality of the food was exactly known and recorded. The cases were typical clinically of scurvy, and Lamb as a result of testing the alkalinity of the blood refutes Wright's statement that the scorbutic symptoms are associated with a condition of acid intoxication which can be easily rectified by the administration of salts of the vegetable acids. Lamb summarizes: "(1) There was no marked deficiency in the alkaline food-stuffs of the dietary before the onset of the symptoms. The diet was common to about 1095 prisoners, and of these only six men developed scorbutic symptoms. (2) There was no diminution of the alkalinity of the blood-serum observed when the symptoms were well marked. (3) There was no improvement in the symptoms either as a result of the giving of a diet consisting of abundant alkaline food-stuffs or on the administration of large doses of lactate of soda."

This suggests the toxic cause theory, that the disease is due to some organic poison in the food the product of decomposition, first suggested by Torup[12] in 1897. Numerous references can be found to complaints from sailors suffering with scorbutic symptoms that the "salt horse" was bad and offensive in odor, and laborers have developed scurvy when working on railroads far from a base of supplies and subsisting on bread and beans and tainted meat. Albertoni previously had shown in some studies in the chemistry of the blood and digestion that intestinal putrefaction is excessive, and Jackson and Harley[13] record the experience of Nansen and Johansen, who spent nine months closely confined in a badly ventilated hut, without any changes of clothing or possibilities of washing, and yet because of living on fresh meat they escaped scurvy. They also state that in the Nares polar expeditions the crews suffered greatly from scurvy, although lime juice was taken daily, because the diet consisted greatly of tinned and salted meat. Experimentally Jackson and Harley fed monkeys on tainted meat, maize, and peas, and another series combining these foods with apples and bananas. They contracted scurvy, while control experiments failed to show typical scurvy.

Horne [14] in criticizing these experiments states that infection was not excluded, a theory held by Berthenson [15] in 1892, and believes that scurvy is an infection of the mouth with various microörganisms from decayed food. Borntraeger,[16] Babés,[17] Teesti and Beri,[18] have all described various microörganisms supposed to cause scurvy, but lack confirmation of their discoveries. Norriski [19] has even asserted that the disease may be contagious. Additional impetus has been given to the infectious theory by Coplans [20] in an analysis of scurvy observed in the Transvaal during the Boer War. He believes that the disease is not due to either the presence or absence of any particular kind of food from the dietary, but rather to an infection for which the food acts as a carrier. Further, the disease prevails in inverse proportion to the hygienic standard maintained, both general and personal. He points out the incidence of scurvy in Europeans and natives, showing the independence of the occurrence of the disease from food factors. Thus, in two units—the native labor corps and the native sanitary corps—the incidence was 16 per cent. in the former and 76 per cent. in the latter, both units being on precisely the same diet, but the sanitary corps were employed in gathering the carcases of animals and burying them in pits.

Coplans further urges the clinical course as further evidence against food being the prime cause of the condition. The cases all commenced as an inflammation of the gums and "improvement or the reverse followed *pari passu* with the improvement or aggravation of the gum condition." In the treatment he notes that cases when seen early could be cured by local means alone without alteration in the diet, and that in advanced cases the stay in the hospital was three times as long when constitutional treatment alone was adopted. Owing to this conflict of ideas upon the causation of the disease by competent observers, the subject is still *sub judice*, and treatment must be carried for the present along lines of hygiene, antisepsis, and diet. It is certain that the incidence of scurvy has declined of recent years since Lind [21] introduced lime juice on board ships, although several writers have ascribed the decline of the disease to improved hygiene, better conditions on ship-board, and a better commissariat in armies, due to the rapidity with which fresh food-supplies can be moved by railroad.

Pathology.—The anatomic changes, while marked, are not important nor characteristic, and, as would be expected, are those produced by the hemorrhage. The general tendency toward ecchymosis, the suffusion into deeper structures, the mucous hemorrhages, are fully described later. The kidneys, bladder, stomach, intestines, lungs, etc., may present the hemorrhagic patches which bled during life, the spleen is soft and enlarged. The muscles and viscera, heart, liver, kidneys, reveal more or less fatty degeneration. There may be serous effusions into the pleuræ, less commonly in the pericardium, and rarely into the peritoneum, and the colon or ileum may present ulcers. Microscopic examination of the tissues has revealed nothing of importance.

Symptomatology.—The disease approaches insidiously, without definite warning or without an acute attack, beginning with progressive loss of strength and weight, pallor, anorexia, and gastro-intestinal disturbances. There is no fever and the pulse is slow and feeble, becoming greatly accelerated during excitation. In addition to the muscular weakness various vague pains are noted in different parts of the body and the patient is drowsy, apathetic, and mentally depressed. The characteristic symptoms then develop, the skin becoming dry, brittle, and scaly, the complexion of a yellowish, muddy hue, and the gingival mucous membrane swollen and spongy, bleeding easily. The mucous membrane appears bluish in spots and so edematous as to rise around the teeth, completely obliterating them, or the gums may become necrotic, particularly about decayed teeth, and ulcerate to a considerable degree, while the teeth loosen and fall from their sockets. In other cases, particularly in children who have no teeth and in the aged who have lost their teeth, the gingival symptoms may be slight or absent; furthermore the severity of the gingival involvement seems to bear no definite relation to the severity of the disease.

In 524 reported undoubted cases of scurvy by four observers,[22] nearly 40 per cent. were without gingivitis. When the gingivitis is marked the breath is foul, saliva dribbles, the salivary glands may be enlarged and painful, the tongue is swollen, and mastication is nearly impossible. A little later a second characteristic symptom develops, the petechial eruptions beneath the surface of the skin. These eruptions resemble ecchymoses or purpura, and appear at first on the lower extremities, particularly about the ankles, and these spread up the legs on to the trunk and arms. They especially appear about the hair-follicles as round, bluish-red spots, not disappearing upon pressure, of varying size, sometimes so large as to appear like bruises, and either developing spontaneously or following blows or bruises. If the hemorrhages are subcutaneous, a distinct elevation of the skin appears, often surmounted by vesicles which may break down and form an irregular chronic ulcer. Hemorrhage into the deeper tissues also occurs, even between the periosteum and bone, and causes a peculiar infiltration of the leg, arm, or trunk, brawny and pitting on pressure, and later becoming of a wooden hardness, the "scurvy sclerosis." Hemorrhages beneath the mucous membrane of the mouth are not often observed, although epistaxis is rather common, and when frequent may contribute greatly to the weakness of the patient. Hemoptysis and hematemesis are uncommon; bloody stools and hematuria occur in very severe cases.

Edema of the ankles and wrists is often seen, and the pleura, pericardium, or rarely the meninges may share the effusion. The pericarditis is a grave symptom and is associated with degeneration of the heart-muscle.

Scorbutic peritonitis is very rare. Pain, swelling, or tenderness in the joints was observed by McGrew [23] in 13 of his 42 cases. While mental depression and headache may be present, meningeal symptoms are not common, convulsions, hemiplegia, night-blindness or day-blindness being only occasionally observed. Necrosis of the bones, separation of the epiphysis, disintegration of recent callus, and fracture (Grünert [24]) may occur. The temperature is variable, usually normal, hemic murmurs are of course present, and the examination of the blood shows a diminished hemoglobin and red cell count, the former being more quickly and more decidedly reduced than the red cells. The average, according to Henry [25] and other observers, is between 3,000,000 and 4,000,000 red cells, although in severe cases the count may be much lower. Suckling [26] reported a case in which the number was 1,290,000, and Talley [27] one with 370,000 red cells and 17 per cent. of hemoglobin. The leukocytes, according to most observers, are usually normal or somewhat reduced, although Stengel [28] says that in scurvy with severe hemorrhage a leukocytosis may be found. The urine is often albuminous, often scanty, of high specific gravity and color. Death from exhaustion, heart failure, septicemia, enterocolitis, or meningitis terminates the advanced cases.

Diagnosis.—The diagnosis is not, as a rule, difficult when a number of persons are affected together, particularly in sailors, soldiers, or prisoners, and especially when the gingival symptoms are marked. Isolated cases are sometimes confused with purpura hemorrhagica, peliosis rheumatica, and occasionally with beri beri or even syphilodermata. Purpura is the most usual mistake, but the association of the insufficiencies or defects in the diet, the hemorrhagic gingivitis, the slight articular involvements, the brawny induration of the subcutaneous tissue, and the dull red-blue color of the macules characteristic of scurvy should serve to make a differential diagnosis possible. In peliosis the macules appear over the whole surface of the body, there is a multiple painful arthritis, no gingivitis, and the onset is commonly marked by sore throat and high fever.

Prognosis.—The prognosis is good, because even in severe cases recovery is possible under appropriate treatment. Convalescence is often prolonged, weeks or even months elapsing before recovery fully takes place, especially in the aged. It has been stated that the hope for ultimate recovery is good if the patient regains the use of the limbs after a few days. During the Civil War the rate of mortality was 16 per cent., but at the present time does not reach 5 per cent.

Treatment.—**Prophylaxis.**—Strict attention to the laws of hygiene in military camps, jails, almshouses, and ships, together with a *varied* diet of fresh meats and vegetables, will prevent the occurrence of scorbutic symptoms where a number of persons are crowded together. The simple administration of lime juice is not sufficient and must always be supplemented by a variety of fresh food. Osler [29] cites the case of a woman with chronic dyspepsia who developed scurvy after living for many months on tea and bread. McGrew [23] found that bread, strong coffee, and meat composed the diet in a large proportion of his cases, and it has been noted in logging camps where bread, molasses, and bacon was the diet. The following enjoy the reputation of being particularly valuable as antiscorbutics: milk, eggs, beets, carrots, spinach, cabbages and "sauerkraut," onions, vinegar pickles, cranberries, and various fruits, especially lemons and limes. A pure water-supply is, of course, absolutely essential.

Curative.—When the disease has developed the treatment is essentially cleanliness, rest, and diet. The local treatment of the gingivitis is of great importance, and, as Coplans[20] has shown, materially hastens convalescence. Antiseptic and astringent mouth-washes and gargles, such as lemon juice, krameria, alum, and a weak solution of silver nitrate, should be used. The cavities and intervals between the teeth should be carefully cleansed. Potassium permanganate or dilute carbolic acid are very useful if mastication is painful; strained vegetable soups should begin the treatment, with lemon or lime juice, and later spinach, green vegetables, water-cress, lettuce, fresh milk, and beef juice. As the patient regains strength and the power of mastication, the varied diet of fresh meat and vegetables should be increased, and even forced somewhat, giving lemons, limes, or an apple between meals. Bitter tonics, strychnin, gentian, etc., may be required if the digestion becomes impaired by the feeding. Iron should be given, lactate of soda has been enthusiastically recommended recently,[9] nitrate of potassium in former years. The constipation is best treated by enemata, diarrhea by astringents, bloody stools by iron, lead acetate, etc., and the administration of calcium chlorid. The stiffened joints and thick, hard, subcutaneous suffusions are best treated by massage.

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CHAPTER XVII.

RICKETS.

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Rickets (Rhachitis, Englische Krankheit) is an acquired disease of young children, which is characterized by changes in the bony system, which produce softening, shortening, and thickening of the bones and enlargement of the epiphyses, and so result in marked deformities. The disease is essentially a medical one, but the resulting deformities frequently demand surgical treatment. This paper will treat chiefly the surgical aspects of the disease.

History.—Probably it has always existed, but the first comprehensive description of the disease was made by the Englishman, Glisson,[1] in 1671. Virchow's[2] article also marks an epoch in our knowledge. Since Virchow's time much experimental work has been done to determine, if possible, its origin, but very little has been added to the knowledge of the finer details of the process.

Etiology.—It may be said in the beginning that the direct cause of the disease is unknown. It has long been known from chemical analysis that the bones of children with rickets contain less lime salts than the bones of normal children, and that the bones are of less specific gravity. Hence it was assumed early that a lack of lime salts was the cause of the disease. Various theories have been developed to explain the cause of this lack.

1. *Theory of Deficient Ingestion of Lime Salts.*—The most natural explanation of the deficiency of lime was that an insufficient amount of lime was taken into the body with the food. There occurs in cattle a disease characterized by a fragility of the bones analogous to the fragility seen in human rickets. Roloff[3] believed that the cause was an insufficient amount of lime in the food of the affected cattle.

Chossat[4] fed pigeons with food from which the lime salts had been removed, and in time produced in those animals fragility of the bones. Voit[5] fed dogs with food deprived of lime and produced fragility and bending of the bones and an enlargement of the epiphyses, that is, a disease resembling rickets clinically, but his proof that the disease is histologically like rickets is insufficient. Other experimenters repeating both Chossat's and Voit's work failed absolutely to obtain similar results. Stilling and Mering[6] fed dogs with limeless food and produced what they called osteomalacia, but which was probably merely osteoporosis. Friedleben[7] fed animals with limeless food and by chemical analysis found that there was a diminished amount of lime in the bones, but he failed to produce the characteristic lesions of rickets. Troitzky[8] called especial attention to the fact that clinical symptoms are no evidence of the existence of true rickets. Miwa and Stoeltzner[9] in a recent careful series of experiments, in which the histologic work is very carefully done, showed that the feeding of animals with limeless food produced osteoporosis of the bones of the animals, but with an absence of true rickety changes. The experimental work shows that, while it is possible by depriving the food of animals of lime salts for long periods to produce in those animals softening and bending of the bones with enlargement of the epiphyses, there is no evidence to show that true rickets can be so produced. Moreover, the absolute failure of the therapeutic administration of lime to cure human rickets is another argument against the correctness of this theory.

2. *Theory of Excessive Acid Formation Producing Excessive Absorption of Lime Salts from the Bones.*—Since experiments show that a lack of lime in the food is insufficient to account for the occurrence of rickets it was assumed that an excess of some acid was produced, which, circulating in the blood, caused an excessive removal of lime already existing in the bones. Haubner [10] ascertained that the fragility of the bones of cattle already mentioned was most marked in regions where the fodder of the cattle was impregnated with the acid fumes from metal-forges. It was assumed that the supposititious acid in rickety children was derived from the fermentation of carbohydrates which produced an excessive amount of lactic acid. It was supposed that this acid was able to remove lime already deposited in the bones, or to prevent lime ingested in the food from being deposited in them. Heitzmann [11] fed animals with lactic acid for long periods and claimed that he produced changes analogous to rickets; in the carnivora the first change was like that seen in rickets, but if the experiment was continued the changes in the bones resembled those seen in osteomalacia. Siedamgrotzky and Hofmeister[12] by similar experiments produced a softening of the bones in experimental animals, but no characteristics of rickets. Other experimenters obtained similar negative results. It has been shown also that in rickets there is no excess of lactic acid in the bones, that lactic acid does not remove lime salts in excess from isolated bones, and that in the urine of rickety children there is no excess of lime salts, so that, on the whole, the acid theory is not proved.

3. *Toxic Theory.*—It has been claimed also that rickets is due to the presence of a definite toxin, produced either by bacteria in the bones or in the circulation or by intestinal bacteria. Spillmann [13] in a very careful consideration of this subject showed that by feeding young animals with the toxin derived from the feces of rickety children suffering from diarrhea rickets was not produced. He also failed to produce the disease by the injection of bacilli from the intestinal canal of rickety children, or by inoculating animals with rickety bones which might be assumed to contain the toxin of rickets. It may be that the cause of the disease is a toxin, which, for some reason, acts especially at the point of most active bone growth, but demonstration of the presence or nature of such a toxin so far has failed.

Predisposing Causes.—*Climate.*—Rickets occurs in all countries, but the frequency of occurrence varies. It is most frequent in cold, damp countries, notably England and Germany. It is less often seen in the tropics or in very cold countries. In regions where it does occur it is more frequent in winter than in summer. This probably is due to the fact that the children of the poor, among whom the disease is most common, live under less favorable conditions as regards air, light, and ventilation in winter than in summer (Kassowitz[14]). In New England the disease is relatively rare in the country and much more common in the city, especially among the children of the poor. The disease affects the sexes about equally and it is commonest in the children of certain races, notably negroes, Italians, and Irish. It may, however, occur in the children of the wealthier classes.

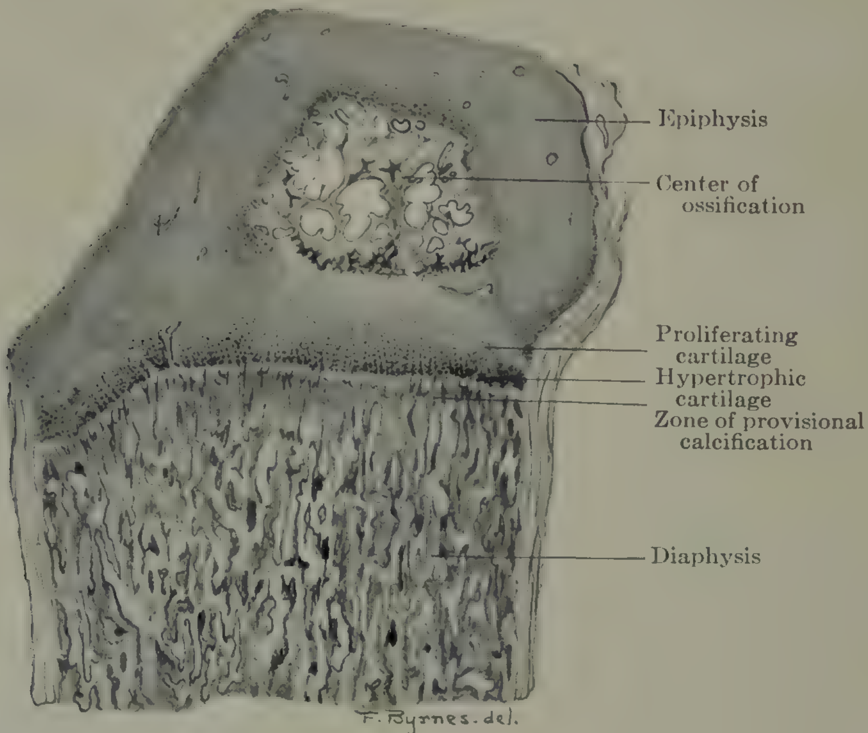


FIG. 150.—A VERTICAL SECTION THROUGH THE EPIPHYSIS AND SHAFT OF LONG BONE OF CHILD AT BIRTH. LOW POWER.

Food.—The method of feeding is agreed by every one to have an important effect upon the occurrence of the disease. The extent to which improper feeding predisposes to the occurrence of rickets is variously estimated by different clinicians. Some go so far as to say that rickets never occurs in breast-fed children, provided the breast milk is normal. The disease is most common among artificially fed children, especially among those who are fed early on large amounts of potato and bread, with very little albuminous food or fruit-acids.

In a large number of the cases there is a history of the use of "proprietary foods." Infants need an animal food. The proprietary foods are almost invariably vegetable foods and have been sterilized. When the vegetable foods are given with milk, the milk is nearly always boiled.

The foods which are made from milk also are sterilized by heat. Heating of foods probably destroys enzymes, the presence of which probably is necessary for proper metabolism. Many of these children suffer from long-continued intestinal indigestion. It can be said that faulty and unscientific feeding is by far the most constant predisposing cause of rickets, but in what way this predisposing cause effects the bony changes is at present not known, nor is there any satisfactory proof of the accuracy of any of the theories most in vogue.

Pathology.—Although various inconstant lesions of the internal organs often are found at autopsies of rickety children, the constant and characteristic changes are those of the bony system. These characteristic changes may effect all of the bones, but generally are most marked in the long bones, and at the junction of the epiphysis, *i. e.*, at the epiphyseal lines (Fig. 150). To appreciate the character and importance of these changes it is necessary to consider the changes which take place at the epiphyseal lines of normal bones.

Normal Ossification of the Long Bones.—The long bones are preformed in cartilage. The transformation of this cartilage into true bony trabeculæ surrounding marrow-spaces filled with cellular marrow begins at the middle of the cartilaginous shaft, and extends in either direction in the long axis of the bone. As a result most of the long bones at birth consist of a bony shaft, or diaphysis, with extremities, or epiphyses, composed of hyaline cartilage in which may exist one or more centers of ossification. Surrounding the bone is a bone-forming layer like the cambium of a tree, the periosteum. The cartilaginous cells of the epiphysis which lie next the diaphysis are constantly being converted into bone, while the epiphysis itself constantly grows by the formation of new cartilage cells. As a result the bone increases in length. The increase in thickness of growing bones depends upon the formation of a layer of new bone in the deeper layers of the periosteum.

The transformation of the hyaline cartilage of the epiphysis into the bony tissue of the diaphysis takes place at the epiphyseal line in a very precise and complicated manner as follows (Fig. 151). The hyaline cartilage of the normal epiphysis is composed chiefly of isolated cartilage-cells which lie in a homogeneous matrix. In the vicinity of the epiphyseal line these cartilage-cells enlarge, proliferate, and lie in groups, which are arranged in columns, extending in the direction of the long axis of the bone, at a right angle to the epiphyseal line. This zone of cells is called the proliferating zone. The cartilage-cells in actual contact with the marrow-spaces of the diaphysis are still larger and form the so-called hypertrophic zone. The matrix between these cells of the hypertrophic zone becomes fibrillated and finally calcified by the deposition of minute granules of lime, thus forming what is called the zone of provisional calcification. As the process continues the marrow-spaces of the diaphysis extend into the space between these provisional calcified cartilaginous masses. The hypertrophic cartilage-cells become converted into bone-corpuscles, just as in the callus in fractures. The provisional calcified matrix is partly absorbed while remnants persist as the basis of new bony trabeculæ. About these trabeculæ appear bone-forming cells (osteoblasts) which are derived partly from the endosteum of the diaphysis and partly from transformation of the cartilage-cells into bone-forming cells. These osteoblasts deposit successive laminæ of new bone about the remnants of the calcified matrix. Into the space between such trabeculæ grow marrow-cells derived from the marrow of the diaphysis. In this way the layers of the epiphysis which lie in proximity to the diaphysis are constantly converted into new bone and the diaphysis increases in length. The gross appearance produced by these histologic changes is characteristic and distinct. The hyaline cartilage is translucent. The layers of the proliferating zone appear somewhat bluer, and the hypertrophied zone makes a narrow clear space which extends in a straight line across the shaft of the bone,

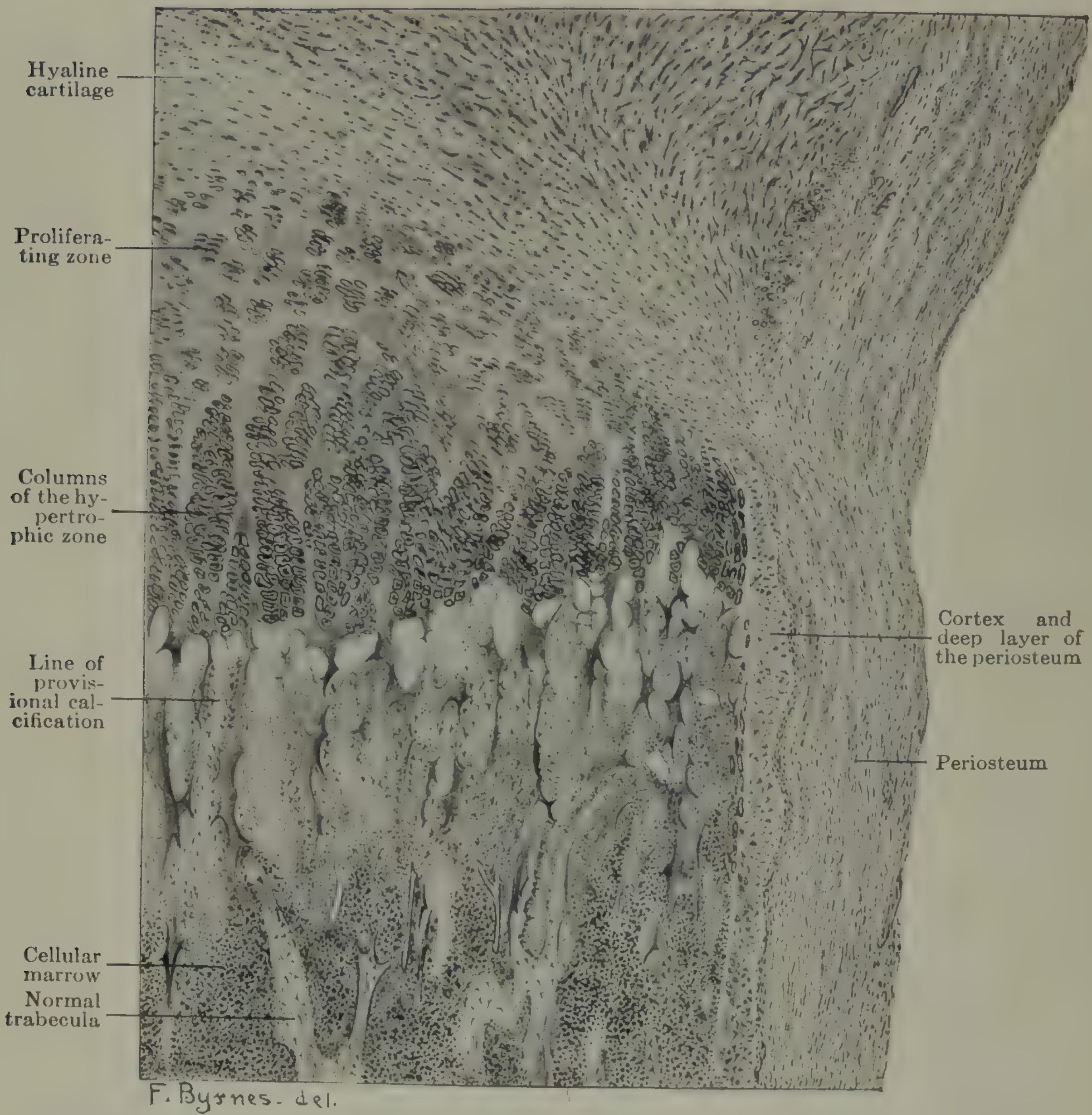

Hyaline cartilage
Prolifera-ting zone
Columns of the hypertrophic zone
Line of provisional calcification
Cellular marrow
Normal trabecula
Cortex and deep layer of the periosteum
Periosteum
F. Byrnes. del.

FIG. 151.—A VERTICAL SECTION THROUGH EPIPHYSIS AND SHAFT OF LONG BONE OF CHILD AT BIRTH. HIGH POWER.

at a right angle to its long axis. Below the clear space of the hypertrophied zone comes a narrow white line (line of provisional calcification), which is parallel to the base of the epiphysis.

Surrounding the diaphysis and the epiphysis is a layer of dense fibrous tissue (periosteum or perichondrium). The deeper layers of the periosteum consist of polygonal cells, similar to the osteoblasts of the marrow, which have the power of forming bone. These periosteal osteoblasts deposit successive layers of dense bone on the outer surface of the cortex of the diaphysis and thus increase the diameter of the bone. This process, if not modified, ultimately would lead to an excessive amount of cortical bone, and to prevent this there is a constant absorption of the inner layers of the cortical bone already formed. This absorption is effected by the giant-cells (osteoclasts) of the marrow (lacunar absorption). Thus by simultaneous deposit of periosteal bone and absorption of the inner layers of the cortical bone the thickness of the cortex always remains relatively the same (Fig. 152).

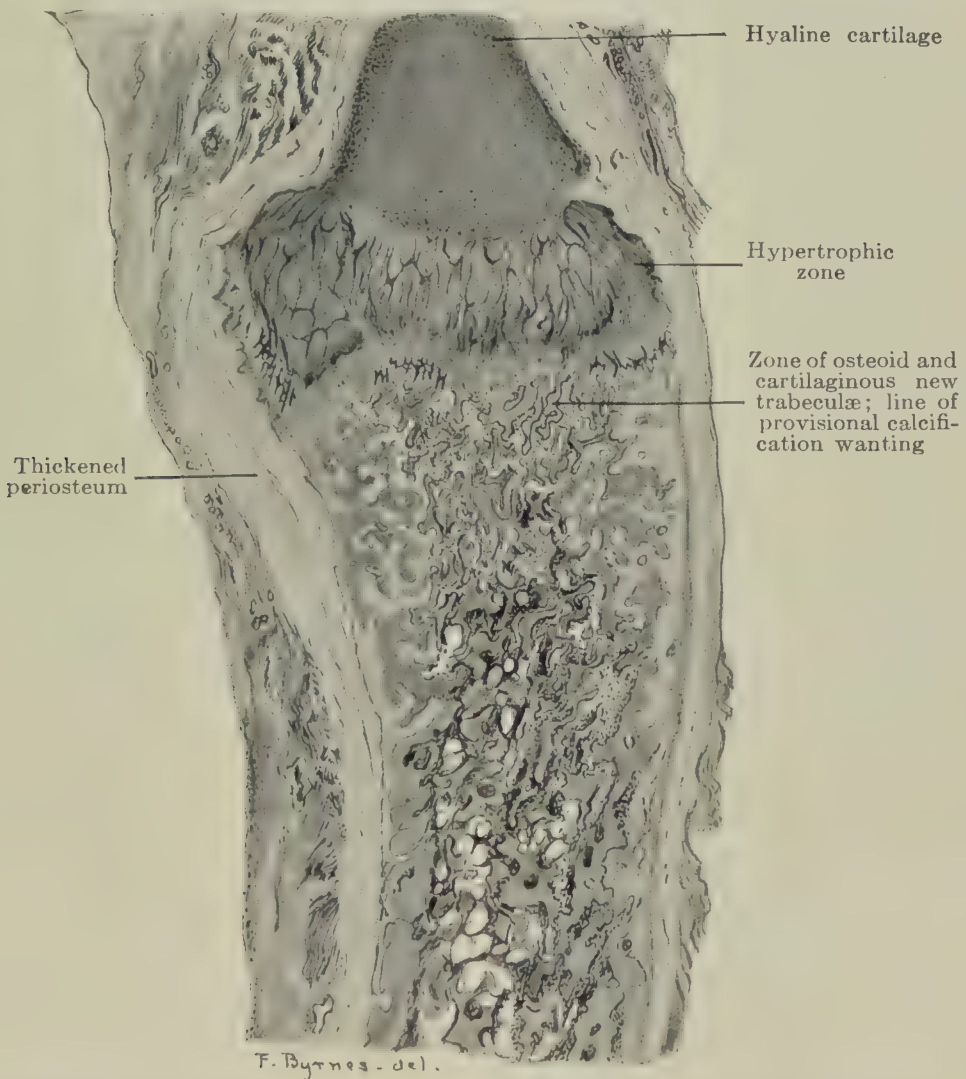

Hyaline cartilage
Hypertrophic zone
Zone of osteoid and cartilaginous new trabeculæ; line of provisional calcification wanting
Thickened periosteum
F. Byrnes - del.

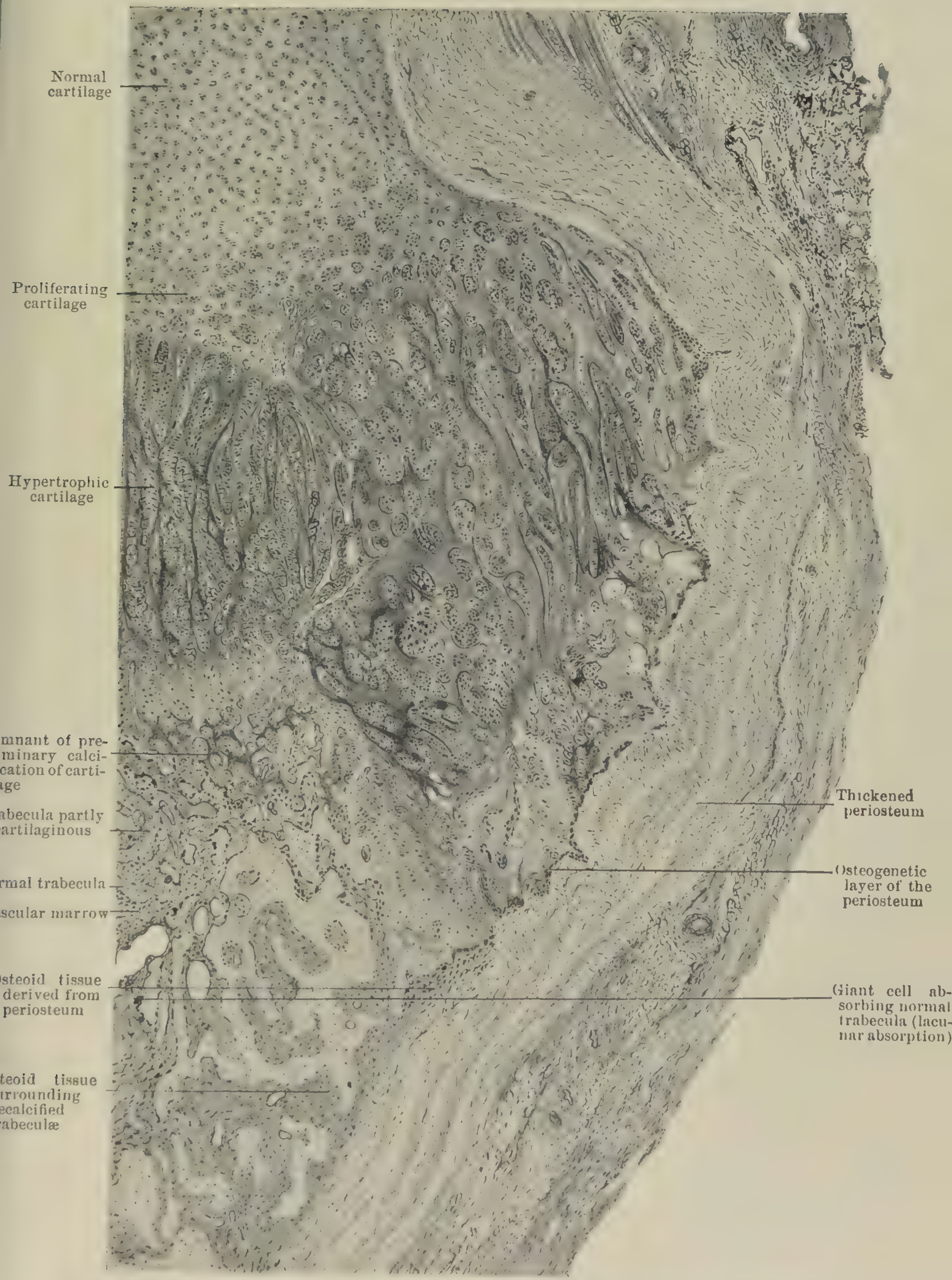
Fig. 152.—Longitudinal Section through Rib at Junction of Rib with Cartilage from a Case of Marked Rickets. Low Power.

Line of Ossification in Rickets.—In rickets the primary and essential bone changes are most marked at the junction of the epiphysis and the diaphysis, *i. e.*, at the epiphyseal line. The chief changes are an increase in amount and irregularity of the zones of proliferating and hypertrophic cartilage, and an absence of the zone of calcification. The zone of proliferation and hypertrophic cartilage is very much wider than usual and the surface which is next to the marrow of the diaphysis is extremely irregular instead of straight. The zone of calcification of the fibrous matrix of the hypertrophied cartilage is almost or entirely wanting. The irregularity of the base of the cartilage is due to ingrowth into the cartilage of blood-vessels and marrow cells from the diaphysis. Besides the absence of the zone of calcification the deeper layer of the epiphyseal cartilage does not undergo the normal transformation into bony trabeculæ. Some of the hypertrophic cartilage-cells persist as cartilage; other portions are transformed into a rather homogeneous material, in which are irregular spaces, like the lacunæ of true bone, producing tissue resembling bone but having no deposition of lime salts. This is the so-called "osteoid tissue." This osteoid tissue usually shows but little evidence of the lamination seen in true bone.

Besides these irregularities there occur changes in the trabeculæ of the diaphysis which have been calcified already. Under ordinary circumstances the growth of the trabeculæ takes place by the successive deposits of layers of new bone upon the old trabeculæ of the zone of calcification by the osteoblastic cells of the endosteum. In rickets many of the old trabeculæ are surrounded by new-formed tissue, usually not laminated, but fibrillated, which resembles bone in its structure, but has no deposit of lime, *i. e.*, "osteoid tissue." As a result, the old trabeculæ become thickened by osteoid tissue which may encroach upon or obliterate marrow-spaces. Also, in course of time, there may occur an absorption of the lime salts from the trabeculæ enclosed in this osteoid tissue, so that the entire trabeculæ composed of calcified and new osteoid tissue become much softer than the original trabeculæ.

There occurs too, in most cases, a marked absorption of the trabeculæ of the diaphysis by bone giant-cells (osteoclasts), so that the actual amount of supporting bony material in the shaft may be very much less than normal (Plate XII). The sum of the changes at the epiphyseal line, then, is a persistence of areas of cartilage, a formation of new trabeculæ of osteoid tissue, a formation of considerable amounts of soft osteoid tissue about the old trabeculæ, an absorption of lime salts from old trabeculæ, and an absorption of old trabeculæ.

Besides these changes at the epiphyseal line there are marked changes in the development of the periosteum. Under ordinary circumstances the periosteum, as has been said, deposits successive layers of true bone upon the outer surface of the cortex of the diaphysis. In rickets the periosteum usually is very much thickened, and deposits an excessive amount of tissue upon the old cortex, but this newly formed periosteal tissue, instead of consisting of true bone, is partly bone, partly cartilage, and to a very great extent osteoid tissue in which no deposit of lime takes


Normal cartilage
Proliferating cartilage
Hypertrophic cartilage
mnant of pre-minary calci-cation of carti-ge
abecula partly artilaginous
rmal trabecula
scular marrow
steoid tissue derived from periosteum
teoid tissue rrounding ecalcified abeculæ
Thickened periosteum
Osteogenetic layer of the periosteum
Giant cell absorbing normal trabecula (lacunar absorption)

LONGITUDINAL SECTION THROUGH RIB AT JUNCTION OF RIB WITH CARTILAGE.
From a case of marked rickets. High power.

place. There may be also a very marked osteoclastic absorption of the inner layers of the cortex, so that the absolute and relative amount of cortical bone is very much diminished. Similar changes may be seen in the periosteum of the flat bones of the skull, leading to the condition known as craniotabes. The marrow in the spaces where new osteoid or cartilaginous tissue is formed is almost always a very vascular myxomatous fibrous tissue, and not true cellular marrow.

As a result of these irregularities in development at the epiphyseal line and in the periosteum various gross deformities are produced in the bones. The bones are short because of the absence of the line of calcification. They are softer than normal on account of persistence of cartilage, the formation of osteoid tissue, and the absorption of existing trabeculæ, and they may be very much thickened because of the excessive formation of soft osteoid tissue by the periosteum. In these bones of abnormal softness various factors act to produce deformities of the bones. These factors are muscular action, the pressure of growing organs upon soft bones, the pressure of the atmosphere, and the weight of the body. These factors being more or less constant produce certain definite gross deformities.

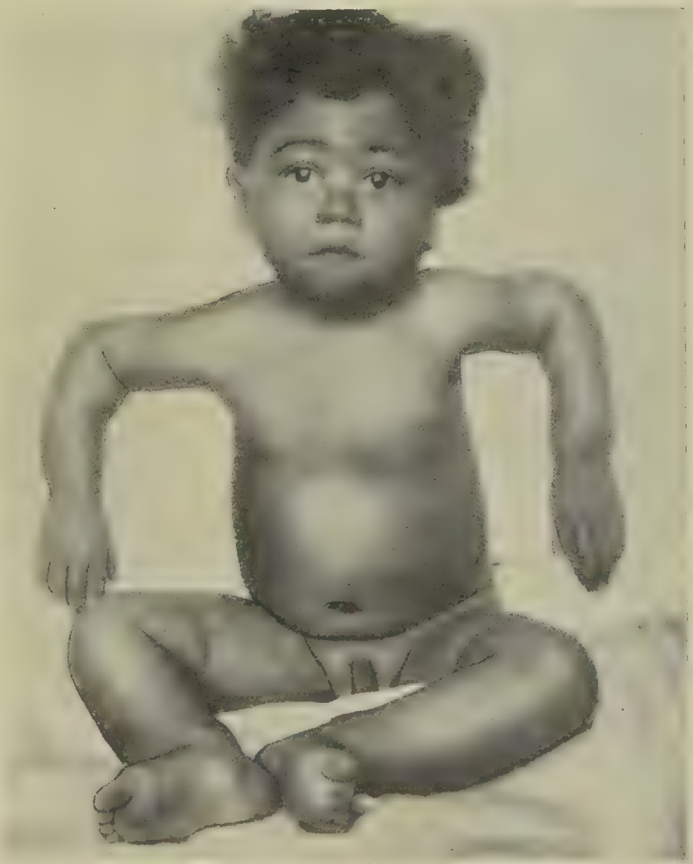


FIG. 153.—RICKETS. MODERATE DEGREE.
Shows square head and square jaw, and enlarged epiphyses of wrists. Abdomen is prominent.

Symptoms.—Rickety children usually are notably flabby and pasty and often show marked protuberance of the belly. A symptom commonly noted very early by parents is the so-called "paralysis of rickets," as the children seem unable to stand or walk. There is, however, no true paralysis and the muscles react normally to electricity. The inability to use the limbs is due partly to weakness and partly to tenderness of the softened bones.

Skull.—The shape of the head in advanced rickets is peculiar and characteristic, the forehead is high, the head square, and there are prominent bosses or nodules, usually over the frontal sometimes over the parietal bones. The jaws may be enlarged from deposit of periosteal bone. In early cases, although there may be no change in the shape of the head, the fontanelles are larger than normal and the sutures between the different bones of the skull may be soft and well marked. Dentition is always very much delayed, and when the teeth do appear they are often very soft, and early undergo decay. In extreme cases some of the flat bones of the skull, usually in the occipital region, by absorption of the original bone and by deposit of new osteoid tissue, may become so soft that they yield to pressure like parchment. In this way is produced the condition known as "craniotabes."

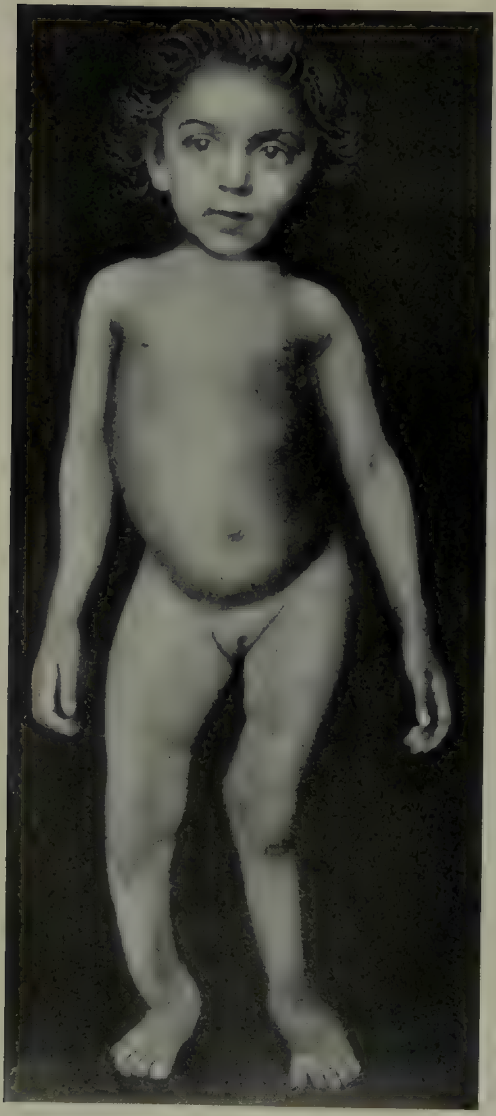


FIG. 154.—RICKETS. SEVERE DEGREE.

Shows characteristic head, deformity of clavicle, rosary, lateral curvature of the spine, anterior and outward bowing of femurs, outward bowing of right leg (bowlegs), inward bowing of left leg (knock-knee), and valgus of both feet. Right tibia shows marked anterior bowing in lower third.

Chest.—The contour of the chest is often markedly changed as a result of the softening of the bones, the pressure of the atmosphere, and the action of the muscles of the chest, notably the diaphragm. The sternum may be prominent and the chest flattened laterally, producing the so-called "chicken-breast." In other cases the sternum is depressed, producing the "funnel-chest." The lower ribs often are elevated by the pressure of the enlarged abdomen. Very frequently there is a transverse depression on either side of the sternum running from the sternum to the posterior axillary line, the so-called Harrison's sulcus. It is supposed that this depression is produced by the muscular action of the diaphragm, although the line of the sulcus is above the attachment of the diaphragm. The earliest and most constant change in the chest, however, is an enlargement of the cartilages at the junction of the ribs with the cartilages, which produces a series of rounded prominences on each side of the sternum, like a row of beads. This is spoken of as the "rosary" of rickets and is one of the very earliest clinical symptoms, frequently appearing as early as the third month. At times the rosary may not appear on the external surface of the ribs, although there may be great enlargement on the inner surface.

Spine.—In mild cases there may be no apparent change in the bones of the spine. In many cases, however, there is a long general curve of the spine, convex posteriorly, giving to the children a peculiar bowed appearance when standing. In some cases this bowing of the spine is so extreme as to resemble the "knuckle" seen in Pott's disease. As a rule, there is no muscular spasm, although in very acute cases some spasm may be present on account of the tenderness of the bones. In some cases the spine, instead of being convex posteriorly, is convex anteriorly in the lumbar region, producing lordosis of the spine. In some cases there may be marked lateral curvature of the spine (scoliosis).

Limbs.—Changes in the shape of the long bones are constant. Nearly always the epiphyses are markedly enlarged on account of excessive proliferation of cartilage in the vicinity of the epiphyseal line. This enlargement appears earliest and most constantly in the epiphyses of the wrists. Bending and deformity of the shaft of the softened long bones occur frequently as the result of gravity and of muscular action upon softened bones. These curves, as a rule, are exaggerations of the normal curves of the bones, although certain conditions, *e. g.*, long-continued faulty position, may produce unusual deformities and curves of the bones. The tibiæ often are enlarged, thickened, and curved. The femurs are often bowed outward and forward. By abnormal growth of the epiphyses the line of the knee-joint may be so altered by overgrowth of one side or the other of the epiphyseal cartilage that knock-knees or bow-legs are produced.

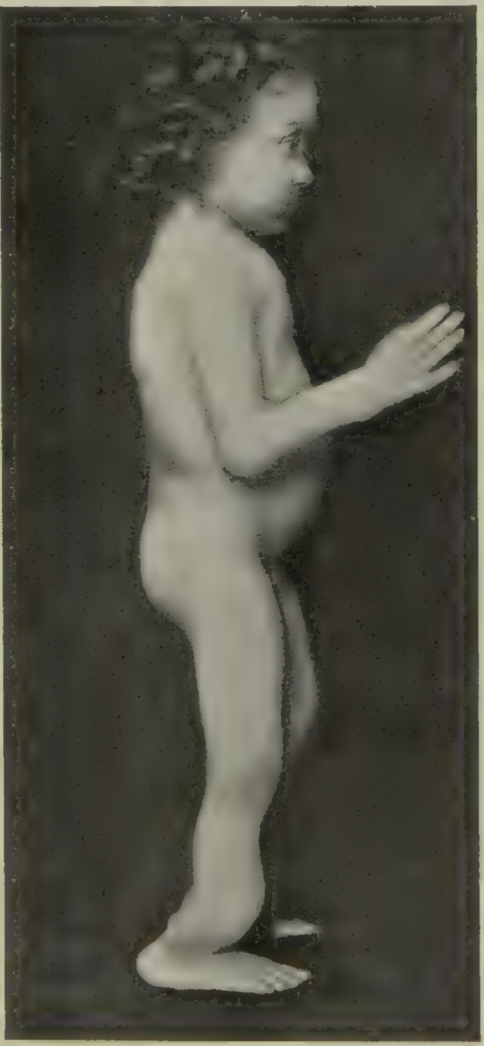


FIG. 155.—RICKETS. SEVERE DEGREE.
Shows prominence of forehead (rickety bosses), rickety curve of the spine, and extreme anterior curve of the tibia.

Pelvis.—By the pressure of the weight of the body and the internal organs upon a softened pelvis, supported laterally by the femurs, marked deformities of the pelvis may occur. Usually the deformity is not recognized in children, but a persistence of the deformity may have very serious results in the after-life of women who become pregnant. The pelvis may be flattened so that its antero-posterior diameter is diminished, "flat pelvis," or the sacrum may project forward, "heart-shaped pelvis."

Other Deformities.—The angle made by the neck of the femur with the shaft may be altered by the pressure of the weight of the body upon the softened neck, so that the neck makes with the shaft a right angle. Often walking upon the softened bones of the foot may lead to alterations in the shape of these bones and the production of flat-foot.

Other Symptoms.—Many children suffering from rickets have catarrh of the mucous membranes and constant diarrhea. Fever usually is wanting. The spleen frequently is enlarged. Anemia is always present.

Nervous Symptoms.—A not infrequent symptom in rickety children is the occurrence of convulsions. The origin of these convulsions is not clear. In some cases the children are subject to attacks of laryngeal spasm, "laryngismus stridulus." These spasmodic attacks come on suddenly and are characterized by a sudden respiratory obstruction followed by an inspiratory "crow." As a rule, these attacks are not serious, but occasionally they are suddenly fatal. Some children show contractures of the muscles of the fingers with flexion of the arms (tetany). Occasionally the spasms affect the muscles of the limbs, leading to extension of the legs and flexion of the toes. It is doubtful if these symptoms are due to rickets. More probably they arise from chronic digestive disturbances.

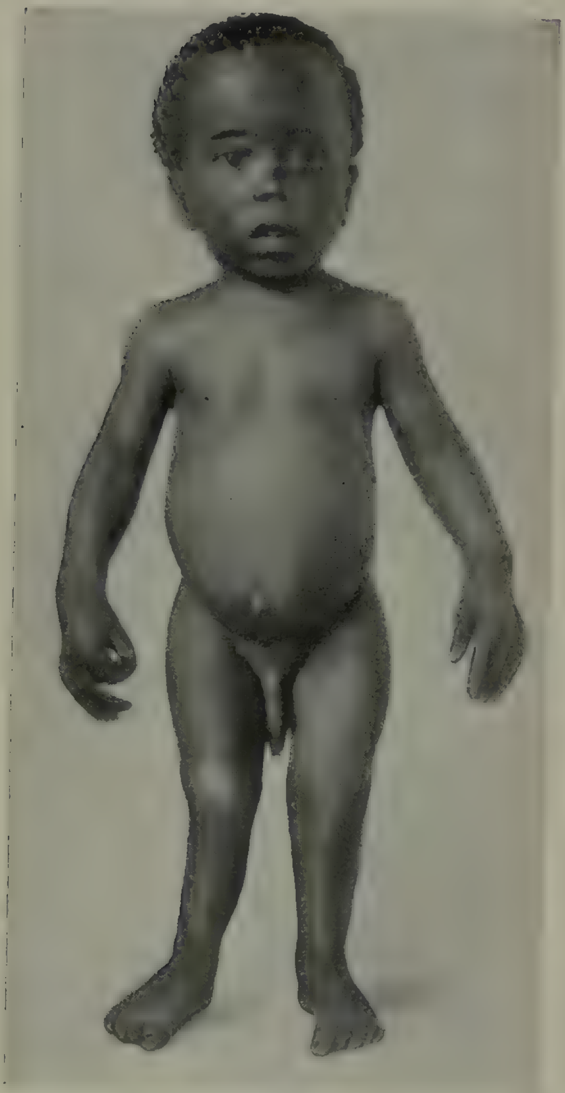


FIG. 156.—RICKETS.

Shows enlargement of the epiphyses of the wrist, bowing of the femurs, and knock-knee.

Recovery.—The disease spontaneously ceases in time, but the results of the disease may persist as permanent deformity if the original deformity of the softened bones was severe. In such cases surgical interference often is demanded to restore the normal contour of the bones. In slight cases the deformity may spontaneously disappear with the cessation of the disease and the growth of the bones.

Prognosis.—The disease itself is not fatal, but many children die of intercurrent diseases, either of the digestive tract or, notably, of the lungs. These children withstand bronchitis, pneumonia, measles, pertussis, and laryngitis very badly. In mild cases, as has been said, the deformity disappears with the growth of the child and the restoration of normal growth of the bones, but if the original deformity is extreme it may persist in adult life.

Differential Diagnosis.—Usually the diagnosis is simple; the large, persistent fontanelles, the delay of dentition, the square head, enlarged epiphyses, and bending of the bones make a clinical picture not easily mistaken. In very young children the disease must be distinguished from congenital syphilis, which sometimes is characterized by tenderness and enlargement of the epiphyses. The history and the absence of secondary syphilitic symptoms usually make the diagnosis easy. Acute rheumatism can be distinguished from rickets by the temperature, and the swelling and tenderness of the joints; in rickets the tenderness is usually in the epiphyses and not in the joints. Acute rheumatism also is rare in children. In Pott's disease deformity of the spine is constant, does not disappear on recumbency, and muscular spasm is marked.

Treatment.—Prophylactic treatment is most important. As has been said, the disease is extremely rare, if it ever occurs, in breast-fed children, provided the mother's milk is normal. It is therefore desirable that young children should be fed upon human breast-milk, either by the mother or by a wet-nurse during the early months. In case this is not possible, great care in artificial feeding is necessary. Undoubtedly the best artificial food is modified cow's milk, *unsterilized*, with a very small proportion of starchy food. As regards air, ventilation, and sunlight, the conditions should be as favorable as possible. After the disease has developed, regulation of the food is the most essential factor. Chronic indigestion must be relieved as far as possible. The child should have a sufficient amount of easily digested food in which starches are in small amount, and which includes meat-juices and fruit-acids, especially orange juice. No drug has been shown to be of especial therapeutic value. The administration of large amounts of calcium seems to have no effect, and phosphorus, highly praised as a specific by some, has not proved successful in most hands. Daily bathing and massage are desirable during the soft stage of the bones. Great pains must be taken to avoid the occurrence of deformities by relieving the bones of the weight of the body as far as possible. The child at this time should be kept recumbent and great pains should be exercised to avoid constant and long-continued faulty position of the bones. As the bones grow firm and the child begins to walk, the application of apparatus (knock-knee brace, bow-leg brace, valgus-plate) may be necessary to aid the bones in sustaining weight or to hold them in normal position. It is undesirable to operate upon the bones during this period of softening, because, even if the operation restores the outline of the bones, they are still soft and deformities may recur as the result of muscular action or weight. After the bones have become hard and firm various surgical operations may be necessary to correct persistent deformities (operations for knock-knee, bow-legs, etc.).

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CHAPTER XVIII.

SURGICAL TUBERCULOSIS.

By John Chalmers Da Costa, M.D.,

PHILADELPHIA.

Definition.—By surgical tuberculosis we mean those various tuberculous lesions of different structures which demand surgical treatment. These lesions are often localized and can frequently be drained, removed, or sterilized.

History.[1]—Phthisis was known even in ancient times. Hippocrates set forth the symptoms, but he placed in one group and regarded as one disease all pulmonary processes characterized by circumscribed suppuration. The view of Hippocrates was held centuries later by Celsus, and was asserted later still by Galen. Hildanus, about the middle of the seventeenth century, described from dissections, pulmonary and mesenteric lesions. Sylvius of Leyden, toward the end of the same century, described pulmonary nodules, which he called tubercula, and which he thought were enlarged pulmonary lymph glands. Sylvius supposed that tubercula were due to a constitutional disposition or disease.

About the year 1700 Magnetus discovered and described miliary tuberculosis; but the discovery attracted little attention, was quickly forgotten, and nearly a century later was made afresh by Stark. In 1785 Reid stated that tuberculous nodules are not enlarged lymphatic glands, but arise from exudates. The distinction between diffuse or infiltrating tuberculosis and the mass of tubercles constituting a nodule was made by Baillie, who also pointed out that cheesy matter forms in each process. Bayle, in the first decade of the nineteenth century, christened the minute nodules tubercles. This able observer traced the development, progress, and fate of tubercles; showed that tubercles are not restricted to the lungs, but may occur in various tissues; maintained that phthisis is of constitutional origin; and asserted that the characteristic of a tuberculous area is caseation.

Laënnec added to our knowledge of tuberculosis. Probably his most important contribution was the statement that scrofula is not a distinct and independent disease, but is glandular tuberculosis. Many years later Cruveilhier warmly advocated the view of Laënnec that scrofula and tuberculosis are identical. Before inoculation experiments were begun, our knowledge of tuberculosis was imperfect and conjectural; our opinions were largely erroneous; and the disease as we understand it today was practically unknown.

Galen believed phthisis to be contagious, and Ballonius, in the fifteenth century, advocated the same view. Many thought that a husband or wife suffering with tuberculosis was liable to infect his or her conjugal partner. Morgagni also believed that phthisis was contagious, and after his day many physicians continued to hold the same belief. Every now and then the view is yet encountered, as a tradition or an opinion, among the general public.

In 1789 Kortum performed inoculation experiments with tuberculous pus, but failed to produce tuberculosis. Laënnec described lesions arising in the wounds accidentally received in performing autopsies on the bodies of tuberculous individuals, and these lesions were evidently what would now be called anatomic tubercles. In 1807 Vienhold published a book in which he maintained the contagiousness of phthisis. Erdt, in 1834, inoculated horses with tuberculous pus, and the animals developed pulmonary nodules. Klencke, in 1843, injected cells from tubercles into the veins of rabbits; and hepatic and pulmonary tuberculosis developed. Villemin's experiments, which were announced to the Académie de Médecine in 1865, attracted great attention. He injected rabbits subcutaneously with material obtained from the lungs of individuals that had recently died of phthisis. The rabbits developed pulmonary tuberculosis, and Villemin asserted positively that phthisis is a specific and inoculable disease. The same experimenter later obtained similar results by injecting rabbits with caseous matter obtained from phthisical sputum, and with tuberculous matter from a diseased cow.[2] Villemin's conclusions were doubted by many and bitterly opposed by some.

A number of experimenters claimed that by inoculating animals with non-tuberculous material lesions identical with those found after injecting tuberculous matter could be produced. It was stated that the implantation of bits of sponge or of powdered glass in the abdominal cavity is followed by what appears to be tuberculous inflammation; that inoculation with ordinary pus produces results similar to inoculation with tuberculous pus; and that the inhalation of pepper, powdered cantharides, powdered cheese, and other substances produces tubercles in the lungs. Villemin's conclusions, however, were confirmed by various observers. Klebs,[3] Cohnheim, and others demonstrated that the apparently opposite results of his opponents were due to faulty technic and to infection from tuberculous material, accidentally present as a contamination; and the studies of this first experimental advocate of the specific origin of tuberculosis stand today undisputed, marking an epoch in our knowledge.

Tubercles were found in lupus by Friedländer; in fungous or pulpy joints by Koster; in enlarged lymphatic glands by Schüppel; and in cold abscesses by Lannelongue. "Friedländer was led by his researches to the conception of a local tuberculosis, which he systematically developed."[4]

From the time of Villemin's paper until the tubercle bacillus was discovered, many observers sought to find the element in inoculated matter really causative of tuberculosis. This element was found by Robert Koch in 1882.[5] It is the Bacillus tuberculosis. Koch clearly, elaborately, and completely proved his case. He showed that the bacillus is present in all active tuberculous lesions; he cultivated the bacteria outside the body; he injected animals with pure cultures, and reproduced the disease; and in the infected animals he discovered the bacilli.

Incidence of Tuberculosis.—Tuberculosis is such a widespread and fatal malady that it constitutes the worst of scourges. It is particularly frequent in northern latitudes, in highly civilized countries, and in populous centers; and enormous numbers die of it. It is not a disease exclusively affecting man, but occurs in many species of domestic animals. Wild animals, when at large, rarely suffer from it; but it may appear among them when in captivity. It is known to occur in captive tigers, lions, panthers, foxes, giraffes, and other animals. Among mammalians liable to the disease are horses, cattle, sheep, monkeys, dogs, cats, swine, and camels. It is by no means uncommon among birds, and occurs in cooped chickens, captive pigeons, domestic turkeys, and caged parrots. Even cold-blooded animals in captivity occasionally suffer with tuberculosis, the disease having been identified in snakes and fish. The question of the identity or duality of human tuberculosis and tuberculosis in the lower animals will be discussed in the section on the bacillus.

Hirsch[6] has pointed out that the average death-rate from all causes is about twenty-two per thousand, and that the average death-rate from pulmonary tuberculosis is three per thousand. Hence the inference that the deaths from consumption alone comprise about one-seventh of the entire number. Of course, these figures do not include the large number of deaths from tuberculous disease of other parts than the lungs; for instance, intestinal, peritoneal, genito-urinary, osseous, and meningeal tuberculosis. When we reflect that the reports of pathologists would indicate that active, quiescent, or healed tuberculous lesions of some sort are found in at least one-third of all autopsies upon persons dying of non-tuberculous conditions, it might seem reasonable to conclude that one-third of the human race suffer from tuberculosis, and that in every civilized community the two-thirds free from the disease, excluding some that are perhaps immune, are constantly exposed to the danger of infection. Lartigau[7] is of the opinion that one-fourth of all deaths among adults are due to this disease, and quotes Evans to the effect that the total yearly mortality of the world is 35,000,000, and that 5,000,000 of these die of tuberculosis.

In spite, however, of this apparent statistical accuracy, these amazing figures are seriously questioned by some high authorities. Cornet[8] disputes the foregoing conclusions. He says that it is certainly true that about one-seventh of all deaths are due to tuberculosis, and that it is also true that some pathologists have found tuberculous lesions in one-third of their autopsies; but that these dead-house figures come from institutions in which the very poorest people have been brought to autopsy, and that among the very poorest there is a much higher percentage of tuberculosis than among the better classes. For instance, he shows that in Austria 11 per cent. of the deaths among the population at large are said to be due to tuberculosis; but that in the public institutions 30 per cent. of the deaths are said to be due to this disease. He also opposed the view that because one-seventh, or even one-third, of the human race die of tuberculosis, that living persons are affected with it in the same ratio, and he states that one could so conclude only if every person that died of tuberculosis had suffered with the disease from the moment of his birth, which we know not to be the case. He says, with obvious truth, that if, at any given time, one wishes to estimate the number of tuberculous individuals in a certain area of population, one should count those that are then suffering with the disease; but that one should not count those that are free from it at that time, even though they may subsequently develop it and die of it. This same authority points out that the number of deaths due to tuberculosis affecting those of a particular age is, year in and year out, about the same for that age. Hence, one can estimate the number of the living suffering with the disease, if one multiplies the number of those dying by the number of years of the disease. In adults, the average duration of tuberculosis is not over three years; and in children, it is even less than this. Cornet concludes that in Prussia, to every thousand non-tuberculous, there are 14.3 tuberculous individuals. Even taking the latter figures as correct, however, one can judge what an enormous amount of tuberculous disease must exist in every community.

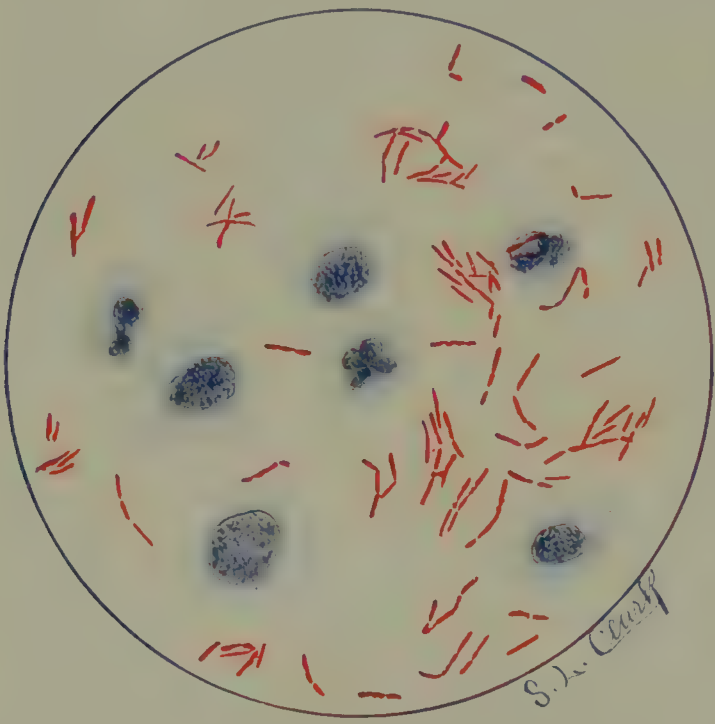


FIG. 157.—TUBERCLE BACILLI FROM SPUTUM ($\frac{1}{16}$ homogeneous immersion).

The Bacillus of Tuberculosis. — The bacillus of tuberculosis was discovered by Koch in 1882. Soon afterward, Hansen discovered the bacillus of leprosy; and Alvarez and Tavel, the smegma bacillus. These three bacilli are in many respects similar, but they are not identical. Each, when stained with anilin colors, retains the stain, in spite of washing with mineral acids; in other words, they are all acid-fast. It was once thought that no other bacteria are acid-fast, but this is now known to be an error. Moeller pointed out that many other varieties of bacteria possess this property.

All acid-fast bacteria have certain properties in common with the tubercle bacillus, although they are not identical with it; and such bacilli are called the bacilli of pseudo-tuberculosis. It may be shown experimentally that they are capable of producing lesions bearing at least a certain superficial resemblance to tuberculous lesions; but that they are not identical with tuberculous lesions is demonstrated by the fact that they tend to cure, and not to destruction of tissue. Some have thought that all acid-fast bacilli are branches from a common trunk; that is, that they are all descended from a common ancestor.

Tubercle bacilli found in different animals differ in morphology and in virulence. Virchow, in 1880, insisted that there are differences between tuberculosis in man and in the other animals. Putz showed that bovine tubercle bacilli are more virulent than human tubercle bacilli, and Klein confirmed these observations. Theobald Smith dwelt upon the difference between the bacteria in different animals. Koch[9] has gone so far as to say that human tuberculosis differs from bovine tuberculosis and cannot be transmitted to cattle at all, and that it is so difficult to transmit bovine tuberculosis to the human being that there is but small danger to man from infected cattle, even from drinking their milk and eating their flesh. Ravenel[10] and others have strongly opposed Koch's contention, and have reported apparently positive cases of the transference of the disease from animals to man. Authorities still differ on this point; but the majority of writers are of the opinion that the two diseases are essentially the same, although the bacilli certainly present distant differences. These differences are probably temporary; and the bacilli are of the same family, but are modified by environment. The bacilli of bovine tuberculosis are doubtless less virulent to man than are the bacilli of human tuberculosis, and the bacilli of human tuberculosis are less virulent to cattle than are the bacilli of bovine tuberculosis.

The bacilli of human tuberculosis are slender, rod-shaped or slightly curved organisms, varying in length from 1.5 to 6 micromillimeters, and in breadth from 0.2 to 0.5 micromillimeters. Some of the organisms may be branched or may possess spur-like projections; hence, it seems certain that the organism of tuberculosis, though called a bacillus, is not a simple bacillus, because a simple bacillus never branches. The organism of tuberculosis is a member of a group of higher fungi—the same group to which actinomyces belong. The organisms are probably non-motile, and are almost certainly without spores. The characteristic staining-reactions, cultivation-phenomena, etc., of the bacillus of tuberculosis are not considered in this chapter.

Distribution.—It seems improbable that the organisms of tuberculosis are saprophytic. Beevor,[11] however, thinks that they occasionally become so; and Woodhead[12] believes that they can live as saprophytes. Practically, the bacteria exist in nature invariably as parasites; and the only sources of infection are man or the lower animals infected with tuberculosis. Wherever there are tuberculous persons or tuberculous animals, the bacteria of the disease, in greater or less number, get into the air. The number that pass into the air is dependent upon the care exercised by the victim or provided for by the one in control, and upon the nature and seat of the bacterial disease. The area endangered by a single tuberculous animal is determined by the animal's habits and wanderings.

The bacteria from an infected person or lower animal may reach the air in sputum, urine, sweat, milk, feces, caseating or purulent material. The purulent matter from an area of mixed infection should be disinfected as carefully as the sputum of a consumptive. The bacteria soon dry and settle in dust; and when lying dried in dust, as a rule, they live but a short time, being destroyed by dryness, oxygen, and sunlight. Koch, Villemin, and others have, however, shown that under certain conditions the bacilli may remain virulent for weeks or even months. Cornet [13] has forcefully exhibited the dangers of dust containing bacteria. Flügge and others have pointed out that when a consumptive sneezes, coughs, or talks, droplets filled with germs are expelled; and that these may float in the air for some time and may cause infection in others. In ordinarily quiet air it is rare for a tuberculous patient to cast a droplet further than 1.5 meters; but if there is a strong wind, or if the effort of expulsion is violent, the droplet may be carried much further. Flugge and his followers regard droplets as more commonly carriers of infection than dust. The bacilli in the atmosphere live for a time, but usually only for a short time, being destroyed by the sunlight, the air, and the dryness. In dark and ill-ventilated rooms the bacilli may perhaps live for weeks in a latent condition.

The common direct source of the bacteria from a given case is the infected part itself; but sometimes the bacteria from the infected part reach the external world by way of the uninfected part. A tuberculous woman in whom the mammary glands are not tuberculous may secrete milk containing bacteria. Flick and Walsh have shown that the urine of a consumptive who is free from genito-urinary tuberculosis may contain bacteria. Adami and Martin, and likewise Koch, have demonstrated that a tuberculous cow may furnish bacterial milk, even when the udder is not diseased. Tubercle bacilli may be eliminated in human bile even when the liver is not tuberculous.

Flies and insects [14] constitute another source of infection. The eating of imperfectly cooked tuberculous meat may also produce the disease. Putrefaction, according to Baumgarten,[15] destroys tubercle bacilli, but most observers think it does not with certainty destroy them,[16] but if it does not destroy them, it seems to lessen their virulence. When an animal is fed experimentally on meat contaminated with the bacilli, these organisms may be found in its feces; and bacilli may be found in the feces of an individual suffering with intestinal tuberculosis. It thus becomes obvious that slaughter-house waste is dangerous.

Avenues of Infection.—The organs most commonly attacked by tuberculosis are the lungs; and it is believed by most observers that infection of these organs is, in the majority of instances, brought about by inhaling dried portions of tuberculous sputum or dust containing tubercle bacilli. When it follows the inhalation of bacilli, the disease is known as *inhalation-tuberculosis.* Experimental infection of the respiratory tract has been produced in animals by rubbing tubercle bacilli into the nasal mucous membrane. When the bacilli are gently rubbed in and the membrane is not damaged by injudicious violence, no disease ensues; but when the membrane is injured, the bacilli may enter and the membrane becomes inflamed and often ulcerates. When the part is damaged, it becomes a point of least resistance in which the vital resistance is at a low ebb. When bacilli thus pass through the nasal mucous membrane the cervical glands—first of that side and then of the other—enlarge and caseate; and, later, the bronchial glands and the lungs become infiltrated. The disease has also been produced in the lungs of animals by causing them to inhale dried and powdered tuberculous sputum or dried and powdered cultures of the tubercle bacillus. Some observers doubt the frequency of inhalation tuberculosis, saying that the laryngeal cilia tend to expel bacilli and not to draw them in, and that in order to reach the air vesicles the poison of tuberculosis would have to be gaseous or be due to bacteria of a specific gravity identical with that of the air (Wright). As Wright says, however, the cilia might be inactive and permit bacilli to pass.

Another source of the disease, and some think the chief source, is the eating of tuberculous meat, the drinking of tuberculous milk, or the consuming of articles of diet upon which the tubercle bacilli have settled as dust and have not been killed by heat. When it so originates, the disease is known as *ingestion-tuberculosis.* Von Behring believes that the tubercle bacillus thus enters the body of every infant, the stomach of infants usually failing to destroy bacteria. When it enters the body it may soon develop or may remain latent for years. Persons who escape tuberculosis do so purely by the reaction of the system (Jonathan Wright).

Tubercle bacilli may be absorbed by the lacteals, when the intestine is perfectly healthy. In fact, Ravenel[17] maintains that primary infection of the intestine is very rare, the tubercle bacilli usually passing through the bowel wall without creating any local lesion. The bacilli pass to the thoracic duct, enter the blood, and lodge particularly in the pulmonary tissues, producing pulmonary tuberculosis; although they may lodge in distant and widely separated portions of the body. In the latter case they tend to lodge at any point of least resistance; and such points may be established by trivial injuries. Severe injuries rarely cause areas of least resistance. A strain of an epiphysis may be followed by osseous tuberculosis; a fracture almost never is. In some cases, after a person has swallowed bacilli, they lodge in the walls of the intestine, causing tuberculosis of the lymph-follicles, or perhaps producing ulceration. In some instances they go directly to the mesenteric glands and cause mesenteric tuberculosis, without producing intestinal tuberculosis, but in most cases, mesenteric tuberculosis is secondary to intestinal lesions. In one case of tuberculosis of the mesenteric and retroperitoneal glands, Fife and Ravenel[18] isolated the bacilli of bovine tuberculosis.

That tuberculosis may arise from inoculation is undoubted. When so obtained, the disease is called *inoculation-tuberculosis.* The most usual victims of inoculation-tuberculosis are butchers, those that make post-mortem examinations, and those that handle hides. I have seen one instance in a physician who had a sore finger at the time when he was making culture-observations with tuberculous material. W. W. Keen saw a case in a pathologist who punctured his finger with a hypodermic needle containing a pure culture of tubercle bacilli. In spite of suction and superficial disinfection of the skin he developed a local tuberculous infection in his finger. Early excision prevented any general infection.

A mother who washed the handkerchiefs into which her tuberculous daughter expectorated suffered from a severe infection of her whole arm through a sore finger. In most instances inflammation and ulceration promptly arise at the site of inoculation; in other cases the wound may completely heal and, after a longer or a shorter time, tuberculous lesions may develop adjacent to it; in still other instances there is no obvious change at the site of inoculation, but the anatomically associated lymph glands become tuberculous. This was the case in the physician to whom I have previously referred.

Kelsh has reported cases in which wounds of the foot were infected with tuberculous dust. In a case reported by Fisher a nurse cut herself with a spit-cup that had been used by a consumptive, and tuberculosis resulted. I saw the case of an attendant in a lunatic-asylum, who had developed an apparently tuberculous ulcer of the skin of the forearm at the point where he had been bitten by a tuberculous patient. Unfortunately, culture-studies were not made. There was no sepsis. The axillary glands slowly enlarged, but the man refused to have them removed. He was finally lost sight of.

Czerny has called attention to the occasional development of tuberculosis through transplanting skin-grafts from another individual. Lartigau[18] says that a large number of cases of inoculation-tuberculosis have followed the circumcision of infants, as carried out by orthodox Hebrew rabbis, who practise suction. In such a case the rabbi must have been the victim of tuberculosis. There is on record evidence which suggests the infection of the genito-urinary tract with tuberculosis through direct contact during coitus, and is has been thought that in certain cases sperm-cells from the tuberculous male may directly convey the disease to the female. In many inoculation-experiments made by rubbing in bacilli infection has not occurred; but in many undoubted instances it has occurred. If there has been little or no local injury, it may not follow; but if there has been definite tissue-traumatism, it is far more certain to follow. It seems probable that occasionally bacilli pass the placenta and enter the embryo. Baumgarten thinks that they may enter the embryo from the placenta and remain latent for a long period, in fact, until late in life. Some reported cases indicate the possibility that congenital tuberculosis may arise on account of tuberculous sperm-cells of the paternal ancestor. But even in some apparently congenital cases it is possible that the bacilli have not passed through the placenta and have not been directly transmitted by the sperm cells, but that there has been transmitted merely a powerful hereditary predisposition to infection and infection occurs unusually early. It seems established, however, that when a woman is tuberculous the ovum may be diseased, and the fetus be diseased from conception; or, if the mother is tuberculous, the bacilli may be directly transmitted to the fetus by way of the placenta. Congenital tuberculosis may exist in many different forms—cutaneous, osseous, glandular, etc.

In some cases it is easy to determine directly the source of the infection in acquired tuberculosis; as when tuberculosis of lymphatic glands follows a tuberculous ulcer of the skin and that ulcer has arisen after injury with a tubercle-bearing object. In other cases it is difficult or impossible to determine the source of infection; for instance, when an infection follows the use of tuberculous food, the source, as a rule, can only be guessed at. Another difficulty in determining the source of the infection is found in the cases in which a very few bacteria enter, and either produce no lesion at the seat of entrance or produce a lesion only after many weeks.

It seems to be established that when tubercle bacilli enter the body and are not quickly killed, and do not become latent in some point of lodgment,[19] they either establish changes at the original seat of entrance, constituting a primary focus, or else pass to the nearest anatomically related lymphatic glands and there establish a primary focus. When a primary focus has once been established, the disease remains local for a considerable length of time and may never pass beyond this point, being cured by encapsulation or fibrous replacement. If it is not restrained locally the disease is then slowly disseminated from this focus. The bacteria enter most readily when there is a wound or an abrasion; but in certain circumstances they are capable of passing uninjured mucous membrane,[20] and even entering undamaged skin.

Certain structures of the body, such as the lungs, are particularly prone to tuberculous infection; other structures, such as the conjunctivæ, are very resistant to it. Any tissue or organ, however, may suffer from it. It seems to have been demonstrated that distribution of the infection through the blood-vessels is rare; although when it occurs, it is rapid and often general: that distribution through the lymph-stream is the common rule; and when it occurs, it is usually slow, and there is a tendency to localization. The advance is in most cases in the direction of the lymph-current, but in some instances it is in the opposite direction. In the latter cases it is probable that the lymph-stream has become blocked, as it occasionally is in cancer, and that there has been regurgitation of the lymph.

Products of the Tubercle Bacillus.—During the growth of the tubercle bacillus, various products are formed. Among those that have been identified are fatty acids, ferments, pigments, toxalbumins, and alkaloids. There has been some dispute as to the exact nature of these products. It seems that there are some bodies of proteid nature that are probably albumoses, and some non-albuminous bodies that are probably alkaloids. When the proteids are experimentally injected, they cause inflammation; when the alkaloidal bodies are injected experimentally, they produce fever. Maragliano,[21] by making a bouillon-culture of tubercle bacilli, passing it through a Chamberland filter, and concentrating it in a boiling-water bath, obtained one group of bodies; and by passing the bouillon-culture through a Chamberland filter and concentrating it at 82° F., he obtained another group of bodies. The first group contained the proteids, already spoken of; and when these were injected into an animal, inflammation followed. The second group contained toxalbumins, which, when injected, lowered the temperature of animals. Maragliano claims that this body that lowers temperature is destroyed by heat. This assertion is denied by De Schweinitz and Dorset.[22] Some other observers who contest the views of Maragliano maintain that the differences in action between these bacillary products are entirely due to differences in the toxic power of the cultures.

It has been certainly determined that the culture-medium in which tubercle bacilli are propagated comes to contain poison, and that there is also poisonous material within the bodies of the bacilli themselves. The poisons present in the culture-medium are called extracellular poisons; those present in the bodies of the bacilli are called intracellular poisons. It is possible, and even probable, that the extracellular poison is merely the intracellular poison that has passed from the bodies of the bacilli into the culture-medium.

A very large number of technical experiments have been made in studying these materials; but the results are, as yet, inconclusive. Various extracts have also been made from bacilli by using different agents. It is believed by Auclair that the fatty substance that can be extracted from the bacilli is the cause of caseation in the tissues, and that the other substances tend to produce fibrous changes in the tissues. When an emulsion of tubercle bacilli is made, there is obtained a poison that is extremely dangerous if injected into tuberculous individuals. This poison resembles tuberculin, but is not identical with it. Koch has made a series of studies to determine the action of the intracellular and extracellular poisons upon tuberculous and non-tuberculous animals.

Tuberculin.—Jaffucci was the first to observe that the injection of numbers of dead bacteria causes symptoms of poisoning in the animal. Inflammation of the kidneys is apt to develop, and not unusually a cold abscess forms at the seat of injection. A number of other observers have confirmed the toxicity of dead bacilli. Koch [23] inaugurated studies to determine the action of the poison of dead bacteria on healthy and on tuberculous animals. The preparation that he first made was liquid and was called *tuberculin*. It was obtained from glycerin-peptone-bouillon cultures of tubercle bacilli. The bacilli were allowed to grow for several weeks at a temperature of 98° F. When a dense cloudiness formed on the surface the bacilli were killed by steam and the material was filtered and concentrated by the evaporation of 90 per cent. of its bulk. A number of different tuberculins have been made by experimenters, and Koch[24] has made several forms himself. This observer has reached the conclusion that neither heat nor chemical action serves to obtain all the poison from the dead bacteria, so his last preparation has been made from dried and ground-up bacilli that have been mixed with water, the bacilli being separated from the fluid with the centrifuge. The fluid that is obtained after centrifuging the preparation is called by Koch "Tuberculin Oberst" (*Tuberculin O.*).

Koch made the discovery that tuberculous animals are much more profoundly affected by the injection of tuberculin than are healthy animals. The reaction after the injection is most marked in and about the tuberculous area; but there is also a definite reaction, as a rule, at the point of injection. The reaction has been obtained in some instances by inhaling dried and powdered tuberculin. The material is, however, best given by hypodermatic injections. Stomach ingestion is altogether unreliable.

After a small dose is given to a healthy animal, there is practically no reaction, except a temporary and ordinary inflammation at the point of injection, and perhaps a trivial and transient fever. In a tuberculous animal, however, there is usually at the point of injection a markedly inflammatory condition; and besides this, a definite reaction in the tuberculous area. The tuberculous region undergoes congestion or actual inflammation; leukocytes gather round it; and there is a strong disposition to death of the part. Hence, the tuberculous focus is apt to break down. If only a moderate dose of tuberculin is given, it seems to be entirely safe; but a large dose may be dangerous. Virchow asserted and many believed that it is apt to cause spread or actual dissemination of the disease. This is possible; but moderate doses in recent cases certainly do not produce such disastrous results, and large doses should not be given.

In addition to the reaction at the point of injection and the inflammatory change at the tuberculous focus, there is a constitutional reaction. The first manifestation of this is a chill, which is trivial when a small dose has been used. In fact, it may be so slight as to be merely a "crawl" (feeling of chilliness). If a large dose has been used, there may be a distinct chill. This condition comes on from four to eight, ten, or twelve hours after the injection. It is accompanied with elevation of temperature. The elevated temperature is accompanied with headache, pain in the back and limbs, rapid circulation, a sense of weakness, anorexia, and restlessness. As the temperature sinks to normal, the other symptoms pass away. The elevation lasts from four to twenty-four hours, or even longer. When given to a non-tuberculous animal, a trivial elevation may follow the injection; but it does not exceed 0.5° C., unless an unusually large amount is administered. If a large amount is given there may be occasionally marked elevation of temperature. It is thus seen that the injection of tuberculin may be a valuable diagnostic proceeding; and the material is used for this purpose, particularly in cattle.

It has been found that in a tuberculous animal body-fluids, serous exudates, and excretions, such as the urine, contain tuberculin; and the injection of such a fluid, obtained from a tuberculous animal, into another tuberculous animal produces a reaction. Poncet believed that blisters sometimes relieve tuberculous joints by withdrawing toxic material. If such serum contains these products, when injected into a tuberculous animal it should produce a reaction, and such a reaction would be an indication that the individual from whom the blister fluid was obtained was tuberculous. This has been done by Mérieux and Baillon,[25] tuberculous guinea-pigs having been injected; their conclusion is that the method is a valuable diagnostic aid. Flick has observed that in from twenty-four to thirty-six hours after applying a blister to a tuberculous patient a marked febrile reaction is noted. This must be due to the absorption of toxic products from the blister, and constitutes a diagnostic tuberculin test. Fig. 158 exhibits a temperature chart made for me by Dr. Landis of the Phipps Institute, Philadelphia. It will be observed that a marked reaction occurred after each application of a blister. Czerny made the important observation that in a tuberculous kidney, although there may have been no bacilli in the urine at the time the injection was made, the injection of tuberculin is followed by the appearance in the urine of numbers of bacilli.

Behring's Views.[23]—In the Congress of Tuberculosis held at Paris in October, 1905, Behring maintained the existence of a curative principle that it is different from antitoxin. He obtains this principle by impregnating a living body with a substance obtained from tuberculous virus. He calls this substance derived from the virus *Tuberculin C.* This material is acted upon by the cells, and its character is changed. The changed Tuberculin C. is called *Tuberculin X.*, a hypothetic substance. The Tuberculin C. of the bacillus is its apparent vital principle. In immunizing cattle by the inoculation of attenuated bacilli, the Tuber-

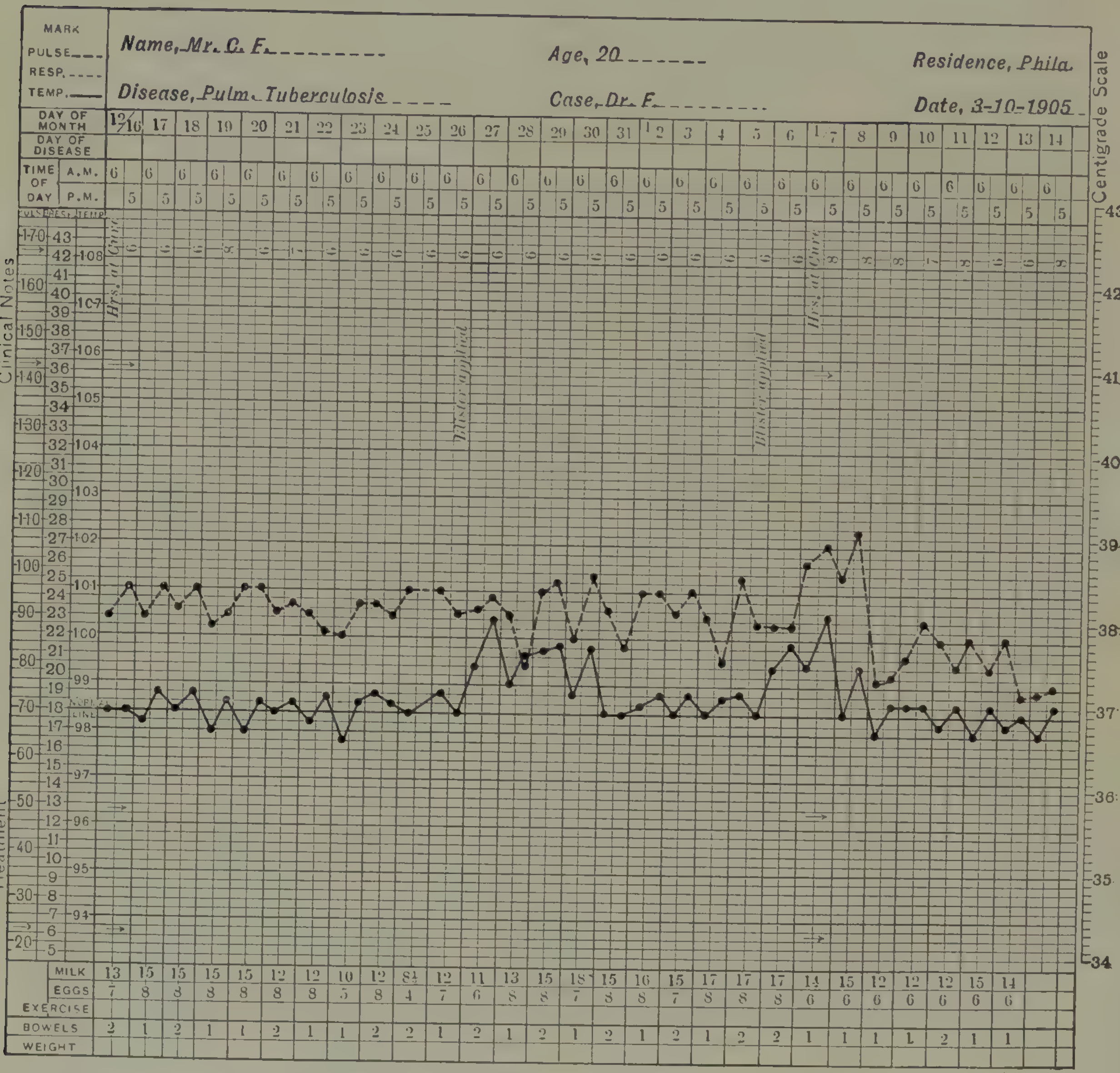

Name, Mr. C. F.
Age, 20
Residence, Phila.
Disease, Pulm. Tuberculosis
Case, Dr. F.
Date, 3-10-1905

FIG. 158.—CHART FROM PHIPPS INSTITUTE TO SHOW THE EFFECT OF BLISTERS ON THE TUBERCULOUS.

culin C. acts on the body-cells, and is responsible for the diagnostic reaction to tuberculin and for the protective reaction toward tuberculosis.

What Behring has striven for is immunity of the cells, rather than of the body-fluids. The method he employs to protect cattle from tuberculosis, he does not employ to protect men, as he is unwilling to introduce living tubercle bacilli, even when attenuated, into human beings. He now renders cattle immune to tuberculosis by injecting human bacilli; these bacilli, by passing through man, become attenuated for cattle. His studies in human protection have been directed to obtaining the Tuberculin C. without forcing the body-cells to the dangerous task of making it. He frees tubercle bacilli of certain substances, and leaves an organism that he calls the rest bacillus. This organism looks and stains like the tubercle bacillus. He treats this bacillus by certain methods that render it amorphous; and this amorphous material (or Tuberculin C.) is readily taken up by the lymph-cells, is changed by them, and changes these cells so that they become eosinophilic or oxyphilic. As the cells are changed, the body becomes immune. This material, Tuberculin C., although it is not living and, hence, not capable of reproduction, can produce tubercles, which do not caseate; and it can also produce infiltration. Tuberculin C. may be used as a remedy in human tuberculosis, to prevent destructive processes. The views of Behring have excited widespread interest; but, as yet, they lack general scientific acceptance.[27]

Resistance of Bacilli.—The power of resistance to different destructive agents possessed by the bacilli of tuberculosis is dwelt upon fully in works on surgical bacteriology. It is sufficient to say here that dryness is antagonistic to them and, as a rule, is soon fatal; that oxygen is antagonistic; and that sunlight is strongly so. We therefore understand one reason why outdoor treatment is so valuable in tuberculosis. Dry heat, the temperature being raised to 202° F., is usually rapidly fatal to the bacilli, although not invariably so; but moist heat at the boiling-point is quickly fatal.

When we consider the effect of chemical germicides, we find that carbolic acid is one of the most powerful. A 5 per cent. solution kills the bacilli in half a minute. Alcohol of full strength comes next in point of power, and about equals an emulsion of iodoform and ether. Corrosive sublimate, in a strength of 1:1000, takes twenty times as long to kill the bacilli as does a 5 per cent. solution of carbolic acid. Formaldehyd is fatal to these organisms, but a long exposure is necessary.[28]

Varying Virulence.—That the infectious power of tubercle bacilli varies is undoubted. Under some circumstances they are powerful for evil; under other circumstances they are moderately dangerous; and sometimes they are greatly attenuated. We know through laboratory experiments that the bacilli may be certainly attenuated; and it therefore seems probable that, as encountered in the atmosphere, the bacteria also vary greatly in their power for harm. Thus, when considering the liability of a given individual to infection, we must remember that the liability depends not only on his own predispositions and antagonisms, and not only on the number of bacteria introduced, but also on the virulence of the individual bacilli.

Immunity.—In all probability there are persons immune to tuberculosis, and I believe we sometimes encounter immunity in those who have been cured of tuberculous disease. The individual cured of bone tuberculosis or gland tuberculosis sometimes seems to have acquired immunity. Persons immune from birth come from a line of ancestors from which the predisposed have been weeded by death. Non-susceptible ones constitute the ancestors of such a line. Immunity may be intensified if proper marriages strengthen the line. Improper marriages, by weakening the resistance, may impair or destroy immunity. Immunity may also be impaired or destroyed in a line by the long continuance of unfavorable conditions.

Conditions that Predispose to Infection.—Any condition of lowered vitality, whether that condition is hereditary or acquired, predisposes to tuberculosis, as it does to many other diseases. It does not predispose in the sense that it of necessity brings the individual into contact with the bacilli of the disease; but it does predispose either because it renders easy the entrance of the bacilli or because, when they have entered, it makes their multiplication more certain to take place. Of course, habits, occupations, modes of life, and places of residence that bring the individual into close and frequent contact with a number of virulent bacteria must increase the likelihood that he will become infected, and must in that sense constitute predispositions.

Hereditary Influence.—I have previously pointed out that congenital tuberculosis occasionally, although seldom, occurs (page 600). There is certainly such a thing as a child being born with tuberculosis; and skin, bone, lung, or other tissue may be involved in the disease. We know that tuberculosis is prone to appear in young children, but this does not mean that the disease in early life is of necessity congenital. It is usually taken to mean that a predisposition to it has been born in or has early developed in the individual. Behring is of the opinion that children become affected with tuberculosis in infancy, through the ingestion of tuberculous food; and that the tuberculosis so obtained remains latent for a longer or a shorter time and then develops. His theory is based upon the known fact that the digestive organs of the child are not able to protect the organism from infection as are the digestive organs of the adult.

Is there such a thing as inheriting a low vital resistance toward the tubercle bacillus particularly as there seems to be a predisposition to scarlet fever particularly? We do not mean, Is there such a thing as great susceptibility to all infections? as we suppose this susceptibility to exist in all weak and sickly persons. What we mean is, Do certain individuals possess a particular vulnerability to tuberculosis? and is such vulnerability hereditary? It has been believed for generations that there is such a thing as a hereditary predisposition to tuberculosis. In fact, this predisposition was once looked upon as almost the only cause of the disease. Of late years, however, the tendency has been to minimize its importance; but in the light of clinical observation and statistical study, it seems impossible to deny its existence.

It is a matter within the observation of all of us that tuberculosis is likely to arise in the descendants of tuberculous persons, and most particularly in the children of a tuberculous mother. A great number of tuberculous patients are able to give a history of antecedent tuberculosis in the family—a father, a mother, a grandparent, an uncle, or an aunt may have been a victim of the disease; and cousins, brothers, or sisters may have it, may subsequently develop it, or may have died of it. It is certain that in 30 per cent. of consumptives one or both parents have been consumptive, and that in 60 per cent. a parent or grandparent has suffered with tuberculosis. The disease, however, is so extremely common that it is impossible to affirm that even a great number of cases of it in one family is due to hereditary. That heredity is at least an element in producing such a state of affairs is suggested by the fact that numerous families exist in which no trace of the disease can be found through several or many generations.

Many observers claim that hereditary influence is apparent in about 50 per cent. of the cases. A disturbing feature in any estimate is that tuberculosis is contagious, and that several members of the family may obtain the disease from one tuberculous member; also that this one tuberculous member, although diseased, may not have been predisposed by heredity. The residence of a family in one house when one member of that family is tuberculous may also account for the development of other cases. A tuberculous mother is more dangerous than a tuberculous father because she is in close and constant contact with the child. That contagion is not the only element, but that there is also such a thing as a family predisposition to contagion, is indicated by the fact that several or many members of a family, though living apart and perhaps far apart, may become victims of the disease. Studies have been made to determine whether there are not marked differences between the children of tuberculous and those of non-tuberculous mothers. We know that some children of tuberculous parents, particularly of mothers, come to present the appearance that the older surgeons called scrofulous; we know that the children of tuberculous parents seem far more apt to develop certain tuberculous lesions than do the children of non-tuberculous parents, but beyond these things we know practically nothing.

Environment.—Very low vital resistance may strongly predispose to tuberculosis, and vital resistance may be lowered by environment. The condition of environment particularly unfavorable to health is poverty, with its attendant evils of bad and insufficient food, damp and unhygienic surroundings, overcrowding, vicious habits, and absence of legitimate amusement and of outdoor exercise. Particularly unfavorable elements in environment are lack of exercise, lack of ventilation, lack of nourishment, dusty atmosphere, and insufficient sunlight. Crowding into damp, narrow, ill-lighted, and unaired houses and rooms, in dusty, dirty cities, is productive of many cases of the disease. The majority of city workers pursue some indoor occupation, and this is one reason that city life predisposes to tuberculosis. The great enemies of the disease are fresh air, nourishing food, sunlight, and outdoor exercise.

It is true that the amount of tuberculosis varies greatly in different regions, and that geographic maps have been made of its distribution. In some regions it is a veritable scourge; in others, it is occasionally encountered; and in still others, it is almost unknown. A careful study, however, leads us to believe that whereas there may be practical immunity at great altitudes and in very dry regions, the disease may, in reality, occur in every place where men dwell; and that the strong predisposition which seems to exist in certain regions is due more to occupation, heredity, and general environment than it is to climate. The life of the town-dweller is the particular predisposition. The inhabitants of Greenland have been thought to possess a racial immunity, and they are free from the disease when in their native country, but the elder Senn has recorded the cases of two Greenlanders that caught the disease when in civilized regions. In each case the disease was apparently cured when the individual returned to the healthy life he was used to in the proper environment of his race.

The Predisposition of Age.—In the first few months of life tuberculosis is uncommon; but as the child grows older, the tendency to this disease becomes stronger, and in children a number of months old the disease is not unusual. It is claimed that 30 per cent. of the deaths occurring in children under two years of age are due to tuberculosis. Toward adolescence, there seems to be a particular susceptibility to tuberculosis of the lungs; whereas tuberculosis of the mesenteric glands is notably common in the first years of life.

The Predisposition of Race.—The colored race, when subjected to the stress of modern civilization, is notoriously prone to tuberculosis, although, as Matas[29] has pointed out, the disease was almost unknown among them before the war between the States, when they were carefully guarded and looked to as valuable property that must not be allowed to deteriorate.

In the United States the Irish seem particularly liable to tuberculosis.

The Predisposition of Sex.—The death-rate from tuberculosis is somewhat greater among males than among females; in fact, some observers regard it as almost twice as great.

The Predisposition of Occupation.—We know that those who follow certain occupations seem to be especially liable to tuberculosis. Occupations that are conducted within doors, in which there is but little muscular activity necessary, and particularly if the worker breathes dusty air, seem especially liable to favor infection. Some inactive occupations, however, may be chosen on account of the fact that the individual does not regard himself as strong enough to adopt an open-air calling; and the weakness that has led him to choose the occupation may be the real predisposition, and the occupation only the apparent one. Statistical studies regarding the death-rate in various occupations have been made by a number of authors.

The Predisposition of Trauma.—We know that an injury may be followed by the development of tuberculosis. An injury of a joint or of a bone seems more liable to be followed by it than are injuries of other parts. Tuberculous meningitis may follow an injury of the head;

tuberculous pleurisy, an injury of the chest-wall; tuberculous epididymitis, an injury of the epididymis, etc. It has been observed that tuberculosis is more apt to follow trivial injuries than severe ones. It is not a dislocation that is antecedent to tuberculous synovitis, but rather a sprain or a contusion of a ligament; it is not a fracture of a bone that is apt to precede the disease, but a strain of an epiphysis or a contusion of the periosteum. Tuberculosis preceded by a direct history of traumatism is unusual, except in the bones and joints and occasionally in the glands. I have seen tuberculosis of the inguinal glands follow a contusion of the groin. In some cases following traumatism, of course, the development of tuberculosis may be a mere coincidence.

In some cases in which the disease has apparently developed in organs subsequently to injury, when post-mortem examination has been made, it has disclosed the existence of an older tuberculous focus. If such a tuberculous focus is at the point injured, the injury has merely roused the inactive focus into activity; if it is distant from the injury, the injury has created a point of least resistance, and the bacilli have lodged there, having come from the old focus. A point of least resistance may at times be influential when no old tuberculous focus, near or distant, exists, owing to the lodgment of stray bacilli from the blood or the lymph. The influence of points of least resistance in determining the location of tuberculous lesions has already been alluded to in discussing inoculation-tuberculosis (page 600).

Other Predisposing Influences.—There are a large number of diseases and conditions which, it seems, may predispose to tuberculosis. The insane are particularly liable to it, probably owing to inactivity and lack of fresh air. Chronic drunkards are also especially liable to the disease, on account of irregularity, inability to take proper food, failure to digest food, exposure to inclemency of the weather, and perhaps from the direct depressing effect of alcohol. The victims of Bright's disease, diabetes, and tertiary syphilis, are particularly prone to develop tuberculosis. Any exhausting malady, such as influenza, measles, or scarlet fever, may predispose; and catarrhal affections of the bronchial tubes frequently precede pulmonary tuberculosis. It was once held that cancer does not appear in the tuberculous. This view was then modified to the extent that it was held that cancer does not appear in the tuberculous organ or viscus; but we now know that cancerous individuals may be tuberculous, and that a tuberculous organ may also be cancerous.

The Term Scrofula.—Scrofula was long thought to be a definite disease. It is now held by many to be synonymous with tuberculosis; consequently, a great number of surgeons have entirely abandoned the use of the term. I believe, however, that it is a useful name. It implies the possession by a person of a type of tissue that has very low resisting-power. These tissues are consequently invaded with ease by the microörganisms of tuberculosis. It may be said that the tissues welcome these microörganisms eagerly and shelter them hospitably.

This condition of tissue-liability is usually hereditary; and it is common to find that one or both parents are tuberculous, are in ill-health, or possess those features that we call scrofulous. A child may, however, be born apparently free from hereditary taint and seem healthy in every way; yet develop this type of tissue later, owing to poor food, bad air, crowding, and general lack of hygienic surroundings.

Some observers maintain that scrofula is simply tuberculosis of bones, joints, and glands; but this is obviously not the case; for a person recognized to be of this type may never develop any tuberculous lesions. Others maintain that scrofula is latent tuberculosis, which will be lighted into activity by some exciting cause; but the objection to the first contention is also the objection to this. I believe that scrofula is not a disease; but that it is a tendency, a disposition, or a predisposition. It is certain that some so-called scrofulous lesions are not tuberculous; and among these lesions we may mention eczema of the face and scalp, ulceration of the cornea, trachoma, and chronic inflammation of the mucous membranes. These lesions seem to result from general ill-health, improper diet, poisoned air, and various bacteria. Subjects that possess the type of tissues known as scrofulous are particularly prone to develop tuberculous lesions, and such a lesion may arise in a part that has been subjected to trivial injury or has been the seat of a non-tuberculous inflammation. The bones, joints, and viscera are particularly liable to tuberculosis.

It is usual to divide people that obviously have the predisposition called scrofula into two types. The *phlegmatic* or common type is the classic scrofula. A person of the phlegmatic type has a stolid expression of countenance, a thick neck, thick lips, a thick nose, thick and coarse skin, a muddy complexion, dark and coarse hair, heavy bones, and an extremely ungraceful figure. His movements are slow and clumsy; his apprehension is dull; it is difficult to awaken his interest; and his emotions are feeble. The other type is more seldom met with. It is known as the *sanguine* type, and the children belonging to this type are often extremely beautiful. The skin is clear and transparent; the eyes are blue and the lashes long; the hair is silky; the bones are long and slender. A child of this type is thin, rather than fat; is extremely precocious; is attractive and graceful; and is of the nervous temperament. In both these types there is lymphatism.

The Status Lymphaticus, the Lymphatic Constitution, or Lymphatism.[30]—This term was devised by Potain to designate a condition often met with in children in whom there is a strong tendency to disease of the lymphatic glands and of other lymphatic tissues, or in whom at birth there was an over-development of lymphatic structures. It is not scrofula, but usually exists in scrofula; and in this condition the glands may be from the start—or, at least, often become—tuberculous. Glandular enlargement is set up by mucous inflammation. The lymphatic enlargements are very persistent; and even if they abate for a time, they tend strongly to recur. The most common lesions of this condition are enlarged lymphatic glands (especially of the neck), enlarged tonsils, and pharyngeal adenoids.

Lymphatism, like scrofula, is usually congenital, but may be acquired.

Children of the lymphatic condition are often rickety, if there exists a combination of causes unfavorable to health, and they are always pallid and anemic. The glands that most commonly enlarge in infancy are the bronchial and mesenteric groups; those that most frequently enlarge in childhood receive the lymph from the pharynx and the tonsil. Some of these children have persistence of the thymus gland and some develop goitre. As a patient becomes older, the lymphatic tissues undergo retrograde change; and lymphatic enlargements are apt to disappear, unless infection with tubercle bacilli has taken place. The glands of the neck, which are so commonly enlarged in lymphatic children, if uninfected with tubercle bacilli, rarely increase in size after the child has reached its seventh or eighth year; and have usually disappeared completely before or by the advent of puberty.

Surgical operations performed upon subjects the victims of lymphatism are often followed by infection, the lymph-vessels and spaces seeming to drink up pyogenic bacteria with eagerness. I have been impressed clinically with this liability to infection. In Gwyer's case there was singularly little bleeding. Gwyer [31] advocates very careful technic in all such operations, in order to lessen the danger of infection. If operating on a gland, he dissects it out until the lymph-vessel is reached, and ligates the vessel before dividing it. If operating on a purulent area, after evacuating it, he rubs in sterile vaselin or iodoform-ointment, in order to block up the lymph-spaces. This seems a questionable method of treatment and of doubtful efficacy. General anesthetics seem to be somewhat dangerous to the victims of lymphatism; and sudden death during anesthesia, or even during natural sleep, may occur.

The Action of the Bacilli in the Tissues.—The bacilli may be killed soon after entering the body. If virulent or in large number, or if the vital resistance of the tissues is low, the bacilli multiply and establish an area of chronic inflammation, the result of which is the formation of granulation-tissue. The cells of a tuberculous focus often have a characteristic arrangement (Plate XIII), constituting what are known as tubercles; and always strongly tend to undergo degenerative changes, because of advancing anemia and coagulation necrosis. The bacilli of tuberculosis are not pyogenic. This point was long disputed, and Tavel and others still affirm their pyogenic power. It seems, however, to have been shown with considerable certainty that they have not such power.

Histology of Tuberculosis.—The histologic characteristic of tuberculosis is a collection of cells known as a *tubercle.* The ordinary or reticulated tubercle contains a distinct reticulum of old connective tissue, and what the elder Senn [32] calls a "network" of branched giant-cells. In the meshes of this network lie the epithelioid cells and the white blood-cells. Occasionally instead of tubercles we find cellular proliferation over a considerable area—a condition known as diffuse tubercle—or else we find a mere fibrinous exudation, the exudation being richly cellular. The mass visible to the naked eye called a tubercle is clear, gray or yellowish in color, and about the size of a mustard-seed. The naked-eye tubercle consists of many microscopic tubercles. The microscopic or primitive tubercle, the most characteristic manifestation of tuberculosis, is composed of three sorts of cells: giant-cells, epithelioid cells, and white blood-cells—a considerable amount of fibrin, as a rule, being contained in this area. When the bacillus lodges in the tissues, the fixed connective-tissue cells multiply by karyokinesis; and a mass of nucleated, polygonal, or round cells is formed. The cells are really of connective-tissue origin, and come chiefly from the endothelium; but they are called epithelioid cells on account of their superficial resemblance to epithelial cells. At this stage of the development of the tubercles, channels for blood exist; but the epithelioid cells lining these channels proliferate and the channels themselves soon become closed, so that the tuberculous area becomes avascular. The obliteration of vascular channels is also hastened by the pressure of proliferating perivascular cells.

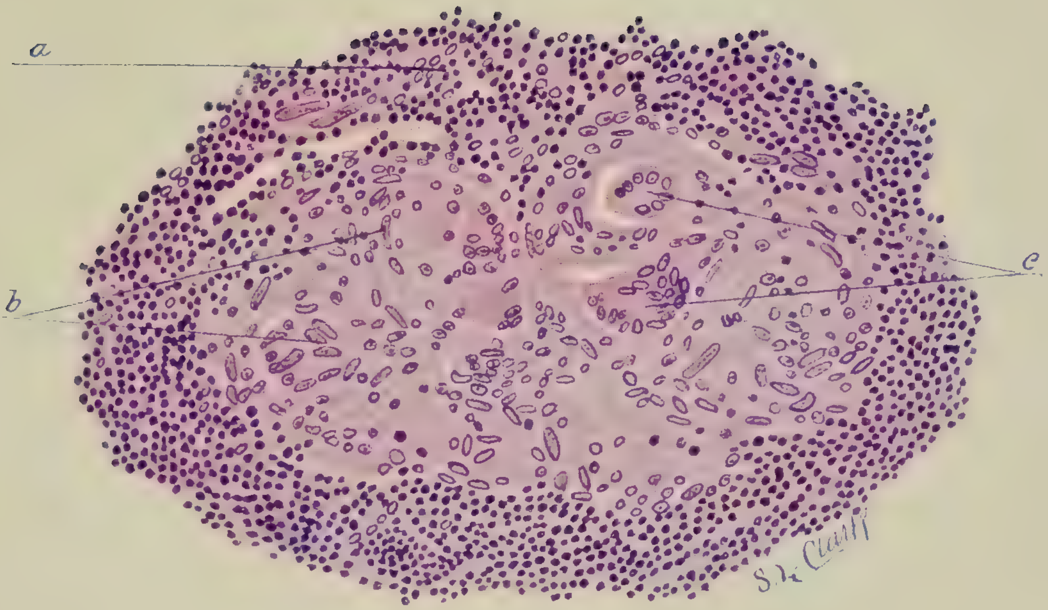
As the blood-supply is being cut off, the epithelioid cells still attempt to proliferate. Some may succeed, but some will fail through want of blood-supply. Those that fail to multiply merely succeed in dividing their nuclei and increasing enormously in size, thus constituting giant-cells. The presence of the irritant bacterial products causes inflammation of the surrounding tissues and a number of lymphocytes gather about the epithelioid cells.

We thus see that a primitive tubercle consists of three cellular layers. Numbers of primitive tubercles constitute the macroscopic, or naked-eye, tubercle, a non-vascular, infective, semi-transparent, gray focus. Owing to the vascular obliteration in a tuberculous area, there is a strong disposition to necrosis and caseation. The giant-cells of tuberculosis are not, as was so long thought, absolutely characteristic of that disease; for exactly similar cells are found in syphilis and other infective granulomata. There are in the tuberculous area, however, inhabitants that are characteristic; namely, the bacteria. These are found in and about the epithelioid cells, and sometimes in the giant-cells.

As the bacilli of tuberculosis grow, they may consume all the available food and die, or may remain latent for a long time. If they die, the granulations become fibrous tissue, and the part is healed. If they remain latent, they are scattered here and there through encapsulating masses of fibrous tissue, and may eventually die or may remain latent and perhaps become active again if a disease or traumatism of the part creates a point of least resistance. The latter course of events is what sometimes follows when an ankylosed and apparently cured tuberculous joint is forcibly broken up. I fancy most of us have seen an active tuberculous process arise in such a joint after forcible attempts at correcting ankylosis.

If there are enough active bacilli to destroy the cells of the granulation tissue, the diseased area caseates. Caseation is a process of coagulation necrosis arising from the action of the microbes upon a non-vascular area. It resembles fatty degeneration, yet it is not identical with it. Caseation starts at the center of the tuberculous focus, and eventually the entire area may be converted into a yellow mass. Caseation forms masses like cheese, which may soften into tuberculous pus by

PLATE XIII.



Histologic Tubercle.

a, Peripheral zone of leukocytes; *b*, Intermediate zone of elongated cells commonly known as epithelioid cells; *c*, Giant cells. The lower line indicates what is probably a giant cell in process of formation.

mixture with serum; may calcify; may become encapsulated in fibrous tissue; or may be replaced by an area of sclerosis. Sclerosis is nature's attempt to heal and repair the part. Spontaneous cure sometimes occurs even when there is tuberculous pus, the fluid portion being absorbed, and the remaining solid portion being encapsulated. Infiltrating tubercle may be due to the fusion of many infective foci, or the process may be diffuse from the beginning. Infiltrating tubercle, like the other form, tends to caseation. The elder Senn points out that an area of tuberculosis may be cured by removing the foci of disease, primary and secondary; and by removing the secondary focus only, if the primary focus has been cured.

Besides the reticulated tubercle, described above, there are two other varieties:

1. The fibrous tubercle contains a vastly greater amount of connective tissue than does the reticulated tubercle, and the connective tissue is much denser. It arises when the bacilli of tubercle die or become attenuated, the tissue-resistance having overcome them, and the embryonal cells of the tissue having ceased to degenerate and having been converted into fibrous tissue by ordinary inflammation. It is an attempt at cure, and leads to the encapsulation of the tuberculous area with scar-tissue. Fibrous tubercles are particularly apt to form when the disease appears in the brain, lungs, liver, kidney, and other organs or in glands.

2. The hyaline tubercle is produced by hyaline degeneration of the reticulum of a reticulated tubercle. It is only the first stage of coagulation necrosis; and whereas the process may be arrested at this stage, it rarely is.

TUBERCULOUS ABSCESS.

(Cold, Lymphatic, Scrofulous, Congestive, Strumous, Wandering, Migrating, or Chronic Abscess—Senkungsabscess of the Germans.)

The condition is best designated by the term tuberculous abscess, as this name makes clear the cause of the condition. The term cold abscess is often employed, because the cutaneous surface above the diseased area does not feel warmer than the corresponding part of the opposite side of the body; in other words, it is called a cold abscess because it does not exhibit heat, and heat is one of the local signs of acute inflammation.

The term lymphatic abscess was formerly used by many on account of the supposed invariable origin of such a condition from the lymphatic structures.

The term scrofulous abscess was used when scrofula was thought to be a distinct disease, of which the so-called abscess was often a part.

The term chronic abscess has been employed to emphasize a common clinical difference between a tuberculous and an acute pyogenic abscess; the chronic or tuberculous abscess is usually a slowly developing process, and is without the signs of acute inflammation. The acute pyogenic abscess is usually a rapidly developing process and accompanied with positive signs of inflammation; nevertheless, as the late Professor Ashhurst said, the term chronic is essentially a bad one, and may convey an erroneous idea.

It refers only to time. All surgeons know that a deep-seated pyogenic abscess may develop with comparative slowness, while a superficial tuberculous abscess may develop with comparative rapidity. Hence, it is evident that the so-called acute abscess may be slow, and the so-called chronic abscess may be rapid in development. The term chronic abscess should be applied to a condition in which there exists genuine pus, arising from pyogenic infection of the granulation tissue of an area of syphilis, tuberculosis, or actinomycosis (the elder Senn[33]). In other words, the true chronic abscess is a condition that results from a secondary infection with pyogenic organisms of some antecedent infective granuloma.

The terms wandering, migrating, gravitating, or congestive abscess have been used on account of the well-known fact that the degenerated products of a tuberculous inflammation are apt to travel to a distance, perhaps to a considerable distance, from the primary focus of disease; for instance, a tuberculous abscess that is found in the lumbar region or in the iliac region may have arisen from tuberculous disease of the vertebræ. In that well-known condition, psoas abscess, the degenerated tuberculous products arise from an area of tuberculous vertebral disease, enter the sheath of the psoas muscle, descend in that sheath, and pass beneath Poupart's ligament to reach the front of the thigh. The idea, however, that their course is determined by gravity is erroneous, as they follow the lines of least resistance even if these are opposite to the direction of gravity.

Definition.—A genuine tuberculous abscess is not an abscess at all, owing to the fact that it does not contain true pus. A true abscess, or an acute abscess, is due to infection with pyogenic bacteria and contains the peptonized material called pus. A tuberculous abscess contains the degenerated products of tuberculous inflammation. An acute abscess is defined as a circumscribed cavity of new formation containing pus. A tuberculous abscess is a cavity of new formation containing the degenerated products of a tuberculous inflammation, which have often reached the recognized point of abscess from some distant focus of tuberculous disease. If a tuberculous abscess is found to contain true pus, there has been mixed infection with pyogenic bacteria. If such mixed infection of a tuberculous area occurs, violent acute inflammation may take place or a genuine chronic abscess, in which there is no evidence of acute inflammation, may form.

Some few observers still believe that the tubercle bacillus is pyogenic. Tavel was of the opinion that the bacilli of tuberculosis have pyogenic properties and Prudden entertained the same view. Nicholas Senn[34] says: "I believe that it can now be considered as a settled fact that the bacillus of tuberculosis is not a pyogenic microbe; that, in the absence of other microbes, it produces a specific form of chronic inflammation, that invariably terminates in the formation of granulation tissue; and that when true suppuration takes place in the tubercular product, it occurs in consequence of secondary infection with pus microbes."

Situations of Tuberculous Abscesses.—A tuberculous abscess is particularly apt to form in connection with tuberculous disease of the lymphatic glands, bones, joints, and subcutaneous connective tissue; but the lesion may form in the brain, any of the viscera, and, in fact, in any tissue of the body.

Age.—Tuberculous abscess may occur at any age, but is most common in childhood. The period of greatest frequency for these abscesses is before the age of twenty.

Contents of the Abscess.—The abscess contains what has long been called scrofulous, curdy, or caseous pus. As previously stated, this is not genuine pus, although it resembles pus somewhat when viewed with the naked eye. The microscope, however, shows that it does not contain genuine pus-elements. In pure cases of tuberculous abscess, we know from repeated examinations of such fluid by staining and microscopic study, by cultures and by inoculations, that pyogenic bacteria are not present. The contents of a cold abscess consist of liquefied, caseated tubercle, masses of coagulated fibrin, and portions of necrotic tissue. The tuberculous material, when viewed with the naked eye, is whitish, yellowish, or yellowish-green, tolerably thick, and devoid of odor. Floating in it are portions of caseous material, which, as the elder Gross said, look and feel like pieces of soft boiled rice. Sometimes the tuberculous material from lymphatic glands and from bone is extremely watery and almost colorless, and contains masses of curds, consisting of tuberculous granulations, coagulated fibrin, and necrotic tissue. In stating that tuberculous pus is free from odor, we must except the material found in tuberculous abscesses of the ischiorectal fossa; but, as a matter of fact, such abscesses exhibit mixed infection with putrefactive or pyogenic bacteria or both. If tuberculous pus is allowed to stand, a thick, curdy mass will settle to the bottom, and a thin, serous fluid will mount to the top.

Formation of a Tuberculous Abscess.—The bacilli of tuberculosis cause chronic inflammation. The tissue-cells, especially the fixed cells, undergo proliferation and granulation tissue is formed. If this new mass of cells is examined microscopically at this stage, it is found to consist of multitudes of cell-clusters, each cluster being known as a primitive tubercle. (See page 611.)

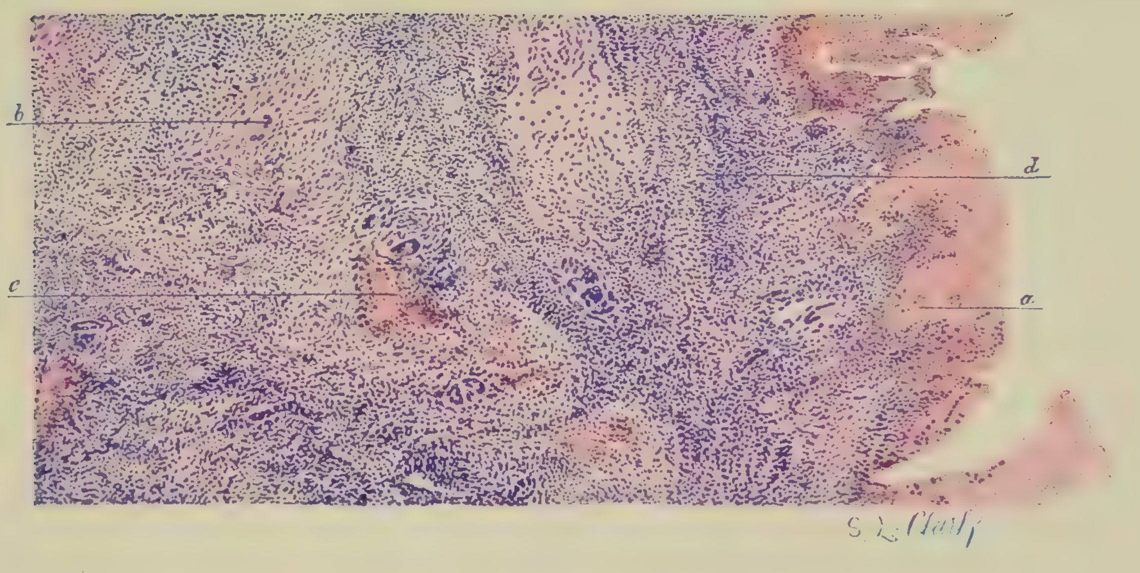
Each tubercle undergoes enlargement. Multitudes of new tubercles are formed, and numerous old ones undergo fusion. The new cells that are formed do not, however, undergo vascularization. Early in their formation blood-channels exist; but these channels soon become closed; and the tuberculous area, at first vascular, becomes completely avascular. The cell-proliferation that in an ordinary inflammation would result in the formation of new blood-vessels, in a tuberculous inflammation results only in the formation of epithelioid cells. It is thus seen that the tuberculous nodule must be imperfectly nourished; as the nodule grows larger and larger, the nourishment grows less and less. Finally, the proliferating endothelial cells cut off the circulation from the adjacent blood-vessels by occlusion of the lumen with new cells, and compression by cellular masses external to the blood-channels also narrows the channels and all possibility of nourishment is abolished. The toxins of the tubercle bacilli, acting upon this area in which the nutrition is greatly impaired, produce coagulation necrosis, and caseation ensues upon this coagulation necrosis. Caseation begins in a great many foci near the middle of the tuberculous nodule. Each caseated area enlarges; and then several, and finally many, caseated areas coalesce. Of course, the tuberculous lesion may be spreading at the periphery while it is caseating at the center. In the caseated material the bacilli perish after a time, for want of nourishment. When an area of caseated tubercle, which is known as a caseated focus, becomes partly liquefied by the addition of serum, caseous or curdy pus is produced; and the lesion is then known as a tuberculous abscess.

The Wall of the Abscess.—A tuberculous abscess is limited by a so-called membrane, which is really a solidification of the tissues due to the compression of their adjacent cells. In a recent case this wall may be soft. In an old case it is dense, fibrous, and uncollapsible. The layer of compressed tissue used to be called the pyogenic membrane, on account of the old theory that it secreted tuberculous pus. This view is, of course, erroneous; as the membrane does not secrete the matter contained in the abscess, but rather surrounds that matter and hinders or prevents its diffusion. As Roswell Park has well said, it is not a pyogenic membrane, but is a prophylactic membrane.

The inner surface of the pyogenic membrane, or of the wall of the abscess, is lined with granulations; and these granulations are tuberculous, and exhibit at various points different stages of the tuberculous process. This layer of granulations is known as *Volkmann's membrane.* (Plate XIV.) The bacilli are not multiplying, and soon perish in the fluid of a tuberculous abscess; although a few living ones may at times be found. They exist in numbers in the granulation tissue of the abscess-wall. When tuberculous pus has been retained and encapsulated, the bacilli soon die. Therefore, because one may fail in making culture-experiments from a doubtful fluid, it is no proof that this fluid has not at one time contained tubercle bacilli. The older the abscess, the less likely are they to be found in the fluid. The same holds true of the condition known as tuberculous empyema, in which one not unusually finds sterile fluid; and the finding of such sterile fluid is regarded as a negative fact in favor of the condition being tuberculous. A sinus, several sinuses, or many sinuses may run out form the abscess-wall. They are lined with granulation tissue of the form that lines the main abscess; and they may pass to distant parts, may penetrate fascia, and may have at their ends secondary abscesses. The wall of an abscess may contain several or many expansions, partly closed spaces, or loculi.

The wall of a tuberculous abscess exhibits, in typical form, the lesions of tuberculosis and their causative bacteria. If the abscess gradually makes its way to some distant place, the tuberculous infection goes with it. If anything happens to destroy this tuberculous granulation tissue or to make breaks in it, without at the same time killing the bacilli lodged therein, it may inaugurate the dissemination of the process; and instead of a local condition, it may cause the patient to develop disseminated tuberculosis. This dissemination may follow spontaneous evacuation, uncleanly operation in which pus germs infect the wall, forcible manipulation which bruises or breaks the wall, and imperfect operation which

PLATE XIV.



WALL OF TUBERCULOUS ABSCESS (so-called Volkmann's membrane).

a, Necrotic tissue bordering cavity; *b*, *c*, Tubercles, the latter showing caseation necrosis in the center. The entire wall is formed of more or less perfect tubercles; *d*, Area of very loose, newly forming fibrous tissue.

removes but part of the tuberculous focus. A not uncommon cause of the dissemination of tubercle is an incomplete operation, and any operation that is performed on a tuberculous area must be thorough and must be done with the most scrupulous aseptic care.

Terminations of Tuberculous Abscess.—A tuberculous abscess may gradually and greatly enlarge, and may finally undergo spontaneous evacuation, either on the cutaneous surface or in some viscus, joint, or mucous canal. It may become encapsulated by fibrous tissue, the fluid elements being absorbed; the tuberculous focus shrinking and remaining caseous; or the caseous area becoming calcified. Again, the area of a tuberculous abscess may be replaced by fibrous tissue; and the condition thus may be permanently cured.

When the focus of tuberculosis is encapsulated by fibrous tissue, and when some bacteria remain living but latent in the walls, the patient may assume for a considerable length of time that he has been cured. As the result of injury or of some more subtle damage, an abscess may reappear at the old seat of trouble. This is due to reinfection from the bacteria that were lying latent in the abscess-wall and did not die. The condition was named by Sir James Paget "residual abscess," because it arises about the remains of an old tuberculous lesion. The rule is that as a tuberculous abscess improves and shrinks, the bacilli finally die through want of sufficient material to feed them. When they do die, the granulation tissue that was previously diseased becomes healthy tissue, vascularized by numerous capillaries. Scar tissue results, and the lesion is healed. The tuberculous abscess may be cured by a surgical operation that removes the primary focus and the secondary focus of disease; or, if the primary focus has itself gotten well spontaneously, the surgical operation attacks only the secondary focus. Of course, in some cases the surgeon operates on a primary focus when there is no secondary focus.

Secondary Infection of a Tuberculous Area with Pyogenic Bacteria.—This occasionally takes place when the abscess has evacuated itself spontaneously. In rare cases it happens when the abscess has not evacuated itself spontaneously and has not been opened by the surgeon, the turberculous area having apparently acted as a point of least resistance to pyogenic bacteria. This, however, is an unusual mode of formation and very seldom occurs, unless a pyogenic process already exists somewhere in the patient's body, to furnish bacteria, which are carried by the body-fluids. When secondary infection occurs, it usually takes place after spontaneous evacuation or during an uncleanly surgical procedure. In some cases violent inflammation and acute suppuration follow such secondary infection; and this condition is very dangerous. The patient may rapidly pass into a state of septicemia; and even if he survives, he will have been placed in the gravest peril of his life. In some cases the suppuration completely annihilates the old tuberculous focus, and thus cures the tuberculous disease; this is very unusual, but sometimes happens, especially in cases of tuberculous cervical lymphadenitis. Secondary infection that causes acute inflammation is so extremely dangerous that it is to be sedulously guarded against; and the older surgeons were so apprehensive of it that they were opposed to operating on a tuberculous abscess, unless it was evidently going to break of itself. In some cases secondary infection does not cause acute inflammation, but does produce a true chronic abscess (p. 613). This condition is not nearly so dangerous as the former.

The dangerous septic condition is apt to arise after secondary infection if the walls of the abscess are thin and poor in fibrous tissue; if they have been damaged by traumatism or strongly irritating chemicals; if the drainage is poor (as is apt to be the case when loculi exist, or when the incision is so small that it becomes blocked with plugs of necrotic tissue or fibrin); if a very imperfect operation has been performed; if the vital resistance is at a low ebb; or if the pyogenic bacteria are peculiarly virulent or have been introduced in large numbers. Streptococci are much more dangerous than staphylococci. In many cases of secondary infection the patient develops what is known as *hectic fever*, a condition characterized by elevated temperature, with an evening exacerbation, a morning remission, and a drenching sweat as the temperature begins to fall; advancing exhaustion, pallor, and rapid loss of flesh.

Secondary Infection with the Bacteria of Putrefaction.—This is a very serious, and often a fatal, complication. It is usually linked with pyogenic infection, produces intense putridity in the wound-fluid, is accompanied with local symptoms of acute inflammation and with the acute and dangerous condition known as sapremic or putrid intoxication (page 621).

Signs and Symptoms.—A pure tuberculous abscess exhibits no sign or symptom that might be regarded as indicating acute inflammation, with the single exception of swelling; hence the designation cold abscess, so frequently applied to it. The skin over the tuberculous abscess does not feel warmer than the skin in the neighborhood or the skin of the corresponding part of the opposite side of the body. The cutaneous surface is normal in appearance, or is actually paler than usual, until the tuberculous process begins to involve the structures just beneath the skin and the skin itself. When this happens, the skin becomes livid; but even then, the color is different from the dusky discoloration of an acute abscess. In the acute abscess, also, there is a glossiness of the discolored skin that is not present in the chronic abscess. The pallid skin over and about a tuberculous abscess is likely to exhibit, here and there, distinctly outlined blue veins. There is rarely any acute tenderness in the region of the abscess, and still more rarely spontaneous pain.

Although pain and tenderness are usually absent at the seat of abscess, there may be pain, and there usually is tenderness, at the primary focus of disease; especially if the primary focus is osseous or articular. If the primary focus is spinal, there is pain in the spine, which radiates along the spinal nerves and may be located by the patient at a point distant from the disease. Bellyache of considerable severity is very frequently noted in Pott's disease of the spine, but the belly is not tender on pressure. Sacro-iliac tuberculosis may be confused with sciatica, owing to the pain in the sciatic nerve; but the nerve is not tender on pressure. The spinal pain of spinal tuberculosis is increased by pressure on the spinous processes of the diseased vertebræ; by concussion applied to the head or the heels, when the spine is rigid; and particularly by movements of flexion. The pain is lessened or, perhaps, abolished by fixation in extension and by rest. In tuberculous abscess resulting from hip-joint disease there may be no spontaneous pain in the hip, but pain in the hip-joint is usually produced by motion. The spontaneous pain is usually appreciated in the knee-joint or to the inner side of the knee. This is due to the obturator nerve, which gives a branch to the hip-joint and also supplies certain thigh muscles, part of the integument of the thigh and leg, and gives a branch to the knee-joint. The pain is felt about the inner side of the knee; it is usually increased by movements of the hip-joint, but the knee-joint is not tender on pressure or movement.

The original focus of disease, if spinal or articular, causes impaired function, which is manifested by the development of rigidity in the adjacent muscles; and this rigidity gives rest by lessening movement. In intra-abdominal tuberculous abscess there is rigidity of the abdominal muscles; in vertebral tuberculosis, rigidity of the muscles of the back; and in tuberculosis of the hip-joint, rigidity of the hip-muscles.

As an acute abscess approaches the surface, the skin not only becomes dusky and glossy, but also becomes edematous; the skin above a superficial tuberculous abscess is not edematous, and the absence of glossiness and dusky discoloration has already been commented upon. In a tuberculous abscess, fluctuation is usually very distinct, the reason being that it is not masked by a great mass of granulation tissue, as it often is in acute abscess; and, further, that there is usually a very considerable amount of fluid present.

One of the chief clinical features of a tuberculous abscess is its disposition to wander to some distant point; in fact, it may suddenly appear at a distant point. I have seen a psoas abscess of considerable size that positive testimony indicated had appeared in that region in the course of a few hours. This tendency to wander is not due to gravity, but is due to the abscess pursuing the line of least resistance, hurried perhaps by sudden muscular movements. The wandering disposition is well shown in abscesses secondary to tuberculous disease of the vertebral column. Such an abscess may be found in the loin, constituting a lumbar abscess; in the iliac region, constituting an iliac abscess; or beneath Poupart's ligament, constituting a psoas abscess. In abscess secondary to tuberculosis of the hip-joint, the condition may appear in the gluteal region, the capsule having given way posteriorly; or in the femoral region, the capsule having given way anteriorly. A tuberculous abscess beneath the deep fascia may make a small opening through the fascia, and a large secondary abscess may form in the subcutaneous tissue. There is thus one abscess shaped like a dumb-bell or hour-glass, the point of narrowing being at the fascial opening and constituting a sinus. Such an abscess is called a "*shirt-stud*" abscess. Not unusually a tuberculous abscess forms several or many sinuses; and at the end of each sinus, an expansion or secondary abscess may form.

In a patient with a tuberculous abscess entirely free from secondary infection the temperature of the body may be normal. The rule, however, is that it is very nearly normal, there being a slight elevation in the evening. The person suffering from a cold abscess is usually weak, pallid, and depressed, with impaired appetite, poor digestion, and unsatisfactory sleep. Examination of the blood rarely shows any noteworthy diminution in the red blood-cells, although it may do so. There is usually a distinct diminution in the hemoglobin, the amount of which is most commonly between 60 and 70 per cent.; but in some cases it is considerably higher, and in others decidedly lower. In very chronic cases, in cases with multiple lesions, and particularly in cases occurring in young children, the number of red cells is decidedly decreased and there is a notable diminution in hemoglobin. If secondary infection occurs, the red blood-cells undergo great diminution in number; and leukocytosis is usually noted. Marked anemia makes the prognosis grave.

If a careful examination is made, the surgeon will in some cases determine that the abscess is the primary focus of disease; but in others he will discover that it has wandered from the original area of disease and that the primary focus of tuberculosis is at a considerable distance. He may find that tuberculous lesions exist in several distant places; and perhaps that important structures, such as the lungs, show areas of disease. It is quite certain, however, that tuberculous abscess may occur in an individual in whom there is no clinical evidence whatever of multiple foci of infection. The tuberculous abscess usually takes a long while—that is, weeks, or even months—to reach the skin or mucous membrane and evacuate itself. When it approaches the skin, the danger of spontaneous evacuation becomes imminent. The approach of the process is indicated by livid discoloration and thinning of the cutaneous surface. Finally, at the thinnest point, a little elevation occurs, constituting the phenomenon known as pointing. This little teat or point ruptures, and the opening gives vent to tuberculous pus.

Spontaneous evacuation is dangerous, because it is very liable to be followed by secondary infection with pyogenic organisms, with the organisms of putrefaction, or with both. Infection with pyogenic organisms in some cases merely leads to the production of a true chronic abscess (page 614), but it may and often does lead to acute inflammation with the ordinary symptoms of acute inflammation, viz., pain, heat, and dusky discoloration. If acute inflammation arises, a characteristic fever develops, and the temperature exhibits a morning remission and an evening exacerbation; and there is a profuse sweat during the night or the early morning. Acute pyogenic inflammation of the cavity of a tuberculous abscess is extremely liable to give rise to fatal septicemia, and infection with the organisms of putrefaction is extremely liable to give rise to fatal sapremia. These points have been discussed on page 617.

Results of Tuberculous Abscess.—A tuberculous abscess may undergo spontaneous cure, which may be permanent. At the seat of an apparently cured tuberculous abscess—perhaps weeks, months, or even years later—another abscess occasionally forms (the residual abscess of

Paget). A tuberculous abscess may remain apparently latent for a very long period of time; and then may diminish in size and undergo cure, or increase in size and rupture. An abscess may undergo spontaneous rupture, and then be cured by suppuration which destroys the superfluous granulation tissue; but, as a rule, when it ruptures spontaneously, it does not tend to cure; either there remains a running area of chronic suppuration, or else the patient's life is destroyed—or, at least, gravely endangered—by an acute septic process. Many tuberculous abscesses are, of course, cured by surgical treatment.

If a tuberculous abscess undergoes secondary infection with pyogenic organisms and a very prolonged chronic suppuration occurs, the patient may develop what is known as *albuminoid degeneration*—the liver, the lymph-glands, the kidneys, the spleen, and other parts becoming enlarged, but remaining smooth. Diarrhea usually develops, and capillary hemorrhages are apt to occur beneath the skin and beneath the mucous membranes. The patient is weak or actually exhausted, is extremely pallid, loses flesh rapidly, and suffers with advancing anemia. In albuminoid disease of the kidneys the albuminoid material is found in the urine; and the symptoms closely resemble those of Bright's disease of the kidneys. This widespread chronic condition is incurable; and usually the patient grows weaker and weaker, and finally dies. In a few cases, if the patient is sent to the seaside or country and lives practically in the open air, it ceases to progress; and the sufferer may become apparently well, although the crippled organ or tissue is never completely restored. It has been thought by some that the condition is the result of the constant flow of pus, which drains the potash salts from the blood and thus dealkalinizes it.

Diagnosis.—The diagnosis is made by observing the tendency to wander, the distinct fluctuation, the absence of signs of acute inflammation, and perhaps the sudden appearance. The discovery of a distant primary focus or of separate and distinct areas of tuberculosis increases the probability that the condition is a tuberculous abscess. The surgeon always examines with the utmost care, to try to discover whether there is a primary focus and whether distant lesions of tuberculosis exist. If the abscess occurs in the neck and there is no evidence of bone-disease, there will probably be enlarged glands or a history of their having been present. Facts of importance in the diagnosis are the absence of leukocytosis, the general failure of the bodily health, the fall in the amount of hemoglobin, and the normal or nearly normal temperature. In a doubtful case the tubular exploring needle is inserted with aseptic care; and the fluid which is withdrawn is carefully examined by differential staining and microscopic studies, by cultivation, and perhaps by inoculation experiments, although one must bear in mind what has previously been stated, that there may be no living bacteria demonstrated, and that the absence of pyogenic organisms and the sterility of the fluid point strongly to the existence of tuberculous abscess. The diagnosis of mixed infection has already been presented.

Prognosis.—This depends upon the general strength of the patient, upon the situation and the size of the abscess, upon whether there are or are not multiple foci of disease, upon whether important organs or structures are diseased or healthy, and upon other facts referred to in discussing the general prognosis of tuberculosis (page 629). A good prognosis may be made if there is no marked anemia; if the secondary focus can be satisfactorily emptied and sterilized, or can be thoroughly removed; if the primary focus can be discovered, reached, and removed; if the patient is not an infant or a very young child; and if the powers of assimilation are good. The prognosis is bad if the patient is an infant or a very young child; and if there are advancing exhaustion, anemia, multiple lesions, lesions of important organs or structures, impaired powers of assimilation, or an area or areas that cannot be satisfactorily sterilized or thoroughly removed. Albuminoid degeneration gives an extremely bad prognosis; and, if the albuminoid degeneration is far advanced, the prognosis is hopeless. The dangers of mixed infection have already been discussed.

Treatment of Tuberculous Abscess.—**The Policy of Laissez Faire.**—The policy pursued by surgeons for many years was to recommend operation only in case the abscess was localized and was unconnected with a primary lesion of the spine, an articulation, or the kidney. What to do when the abscess was a secondary evolution from such a primary focus was involved in great doubt. Many surgeons advocated letting the abscess alone and permitting it eventually to empty itself spontaneously, believing this natural method to be safer than surgical drainage. I have previously pointed out the dangers of spontaneous evacuation; and we should further remember that pointing may be deferred for a long time, and that, during the necessary and wearisome delay, there is grave danger that the abscess and also the primary focus of the disease may spread. There is likewise considerable danger that tuberculosis may develop in some distant part or parts of the body.

It was considered a notable evidence of radical advance, when surgeons began to advocate interference in certain selected cases of secondary abscess. It came to be thought by many that in a case secondary to tuberculosis of the spine, operation should be performed when the spinal condition became quiescent, this quiescence being indicated by the abatement of pain, the cessation of increase in the deformity, and the evidence of a gain in flesh and strength. In a case in which the symptoms have thus abated, the abscess-wall is firm and fairly thick; the tuberculous fluid contains few living bacilli, and probably no virulent ones; and the danger of the dissemination of infection after operation is at a minimum. Unfortunately, however, the prolonged delay usually necessary when such a plan is followed may be disastrous. During this period, the abscess may widely extend its area and hopelessly damage important structures; and distant secondary, and sometimes multiple, tuberculous lesions may develop. It thus becomes evident that delay may be not only disastrous, but actually fatal. Consequently, the let-alone plan, which is largely the trust-to-Providence system, has been abandoned; and all these abscesses, with but few exceptions, are operated upon.

Aseptic Incision and Drainage.—With the introduction of antiseptic surgery, it was generally assumed that even tuberculous abscesses of large size might be confidently attacked without fear of secondary pyogenic or putrefactive infection. This view was found to be erroneous. It is quite true that an abscess that is localized and has not wandered from a distant focus may be so treated with safety; but an abscess secondary to articular, osseous, or visceral disease should not be so treated. The tuberculous wall cannot be completely removed; and although, if every care is taken, infection will not happen at the time of operation, it is very apt to arise during subsequent dressings, or when the dressings remain for some time in place after they have been soaked with discharge. We may, then, lay it down as a rule that a secondary focus should not be treated by simple incision and drainage; but that a localized abscess that is itself the primary focus, being unconnected with articular, osseous, or visceral disease, may be so treated.

When the incision has been made, the abscess-wall should be thoroughly scraped with what is known as Barker's flushing gouge, a sharp-edged spoon that has associated with it an irrigator; so that irrigation and curettement go hand in hand. The material used to irrigate is hot normal salt solution. Treves's douche scoop is a similar instrument. After the wall has been scraped and irrigated, the incision is only partly closed by stitches; and strands of iodoform gauze are introduced, in order to pack the walls apart and to permit of drainage. When healthy granulations have been formed packing is abandoned and but a strand or two of gauze is applied to secure drainage.

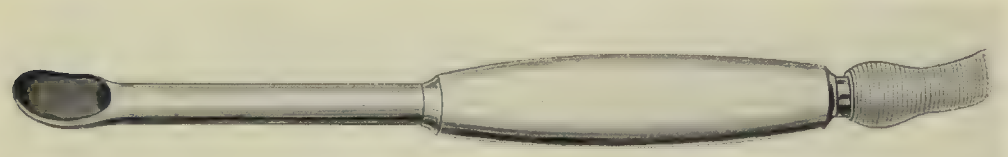


FIG. 159.—BARKER'S FLUSHING GOUGE.

Small tuberculous abscesses that are superficial are always treated by aseptic incision. After incising an abscess that seems to be superficial, the surgeon should always make a careful examination, in order to be sure that he has not been in error, and that there is no connection with another focus. If he finds such a connection, he may perhaps consider it desirable to throw the two foci into one by incision, to cleanse the abscess cavity, to rub its walls with gauze, to insert emulsion of iodoform, and to completely close the wound with sutures. This method of procedure will be spoken of later.

After having determined that there is no other focus, the surgeon should also see whether tracking sinuses exist; and if they do, he should slit them up and scrape them. He should likewise see whether there are loculi in the abscess-wall; and if there are, they should be widely stretched and scraped. He should furthermore see that he is not dealing with a shirt-stud abscess, the main part of which, of course, is beneath the deep fascia.

If he finds a shirtstud abscess, he must incise the deep fascia and treat the cavity beneath as he has treated the one above.

If the skin over an abscess is much discolored, and the abscess is on the point of breaking or has broken, the discolored skin must be cut away. If this is done, the gap will be replaced by healthy scar tissue; and the scar will not be gravely disfiguring. If the discolored skin is not cut away. an irregular, livid, jagged, and disfiguring scar will result. This point is of the greatest importance when the surgeon is dealing with a tuberculous abscess on the neck of a girl or a woman.

Evacuation with the Aspirator-needle, followed by Irrigation and the Introduction of Iodoform.—This plan of treatment was introduced a number of years ago by Verneuil, who removed the tuberculous fluid by means of an aspirator, and then introduced a solution of iodoform and ether. This method was found not to be altogether safe, the ether vaporizing from the heat of the body and sometimes rupturing the wall of the abscess. There is also some danger that iodoform-poisoning may occur, and the injection often causes great pain. Billroth substituted the emulsion of iodoform and glycerin, in a strength of 10 per cent.—a material still used by many. Krause prefers the following 10 per cent. mixture of iodoform: 50 parts of powdered iodoform, 23 parts of mucilage of gum Arabic, 83 parts of glycerin, and 500 parts of distilled water. As a matter of fact, however, Billroth's 10 per cent. emulsion is just as satisfactory as Krause's more elaborate formula. It is sterilized by careful boiling. It is well known that iodoform retards the growth of the bacillus of tuberculosis, and that its efficiency depends largely upon its acting in a region from which air is excluded. This inhibitory action on the growth of the organisms when air is excluded is extremely powerful and, by the retention of the iodoform in a closed cavity the drug is disseminated over the entire abscess-wall; and its action is greatly prolonged.[35]

The entire operation of tapping, irrigating, and injecting the abscess must be carried out with the most complete aseptic care. The aspirating trocar is inserted through sound skin; is carried along directly under the skin for an inch or more, as Senn advises; and is then plunged into the abscess-cavity. When it enters this, the stilette is withdrawn; and the outflow of the tuberculous material is aided by very gentle pressure. If the tube becomes blocked with masses of fibrin or shreds of necrosed tissue, it must be freed by introducing a wire or forcing in a stream of sterile fluid.

When the tuberculous matter ceases to run, a very warm solution of boracic acid, of a strength of about 3 per cent., or a very warm normal salt solution, is thrown into the abscess to cleanse its walls. It may be thrown in with an ordinary fountain-syringe, the hose of which is attached to the canula; or, better, by the special injection-syringe devised by the elder Senn (Fig. 160). Our object is to overdistend the abscess-cavity, as was long ago recommended by Mr. Callender; so that every portion of the wall may be reached by the fluid. When the cavity is overdistended, the fluid is allowed to run out. Fresh fluid is then introduced; and these manœuvers are repeated until the fluid emerges entirely free from any solid material. Then the iodoform emulsion is thrown into the abscess and is allowed to remain.

In a certain percentage of cases the introduction of iodoform has been followed by symptoms of poisoning. Therefore the surgeon must be careful; and, at the first operation, he must use only a small amount. At subsequent operations, if no harm has resulted, he may perhaps increase the quantity. The ethereal solution is more dangerous than the emulsion. In the adult not more than eight or ten drams of the emulsion should be introduced at the first operation; and in the child, not more than half this amount.

After the emulsion has been thrown into the cavity of the abscess, the wound in the skin is covered with a small piece of sterile absorbent cotton soaked in iodoform-collodion. A compress is made of fluffed-up gauze and laid upon the skin above the abscess-cavity, and the walls of that cavity are then approximated by the application of a roller bandage. The part affected must be put at absolute rest, and in most cases it is desirable to confine the patient to bed.

It is seldom that one injection cures. The procedure commonly has to be repeated. Usually, it will be found in a week or so that the cavity has partly refilled. A second operation is then performed. If the patient is really getting better, it will be found that the fluid is thicker at the second than it was at the first operation. If half a dozen tappings do not cure, then this plan should be abandoned. An abscess with thick, rigid, uncollapsible walls should not be treated by aspiration and injection, as after emptying the cavity it is impossible to bring the walls in contact, or, is at least impossible to hold them in contact.

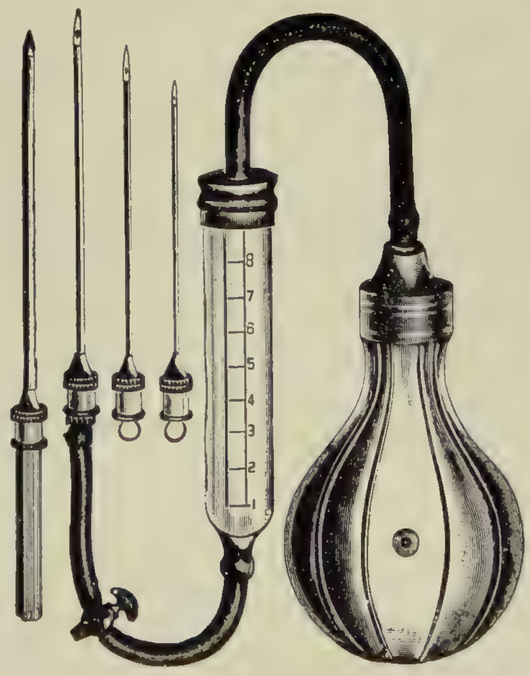


Fig. 160.—Senn's Injection Syringe.

Incision, Cleansing, and Suture.—If the aspiration method has failed, or if, owing to the large size of the abscess, it has not been used, one can practise incision, irrigation, and immediate suture. This method, too, is unsuited to a case with a very thick and rigid wall. When applied to suitable cases, it frees one from the danger of secondary pyogenic infection which danger attends the use of a tube or packing.

The most dependent portion of the abscess is incised. The walls are scraped thoroughly with Barker's spoon, which scraping, it will be remembered, is associated with irrigation. The walls are then rubbed thoroughly with bits of gauze, which act as rasps or files. The part is irrigated again; hemorrhage is arrested by pressure; iodoform emulsion is introduced; the skin-wound is sewed up; gauze dressings, compresses, and bandages are applied; and complete rest is given both the part and the patient. One such operation occasionally cures an abscess; although perhaps it may be necessary, several or many weeks afterward, to reopen the area and repeat the procedure, when it will usually be found that the cavity is much shrunken and greatly improved.

The Incision and Removal of a Primary Focus of Tuberculosis.—If the treatment with iodoform fails; if it has not been used on account of the rigidity of the abscess-walls or the great size of the abscess; and if the primary focus of tuberculosis can be reached and removed surgically, the surgeon should undertake an operation that not only removes the pyogenic membrane from the secondary abscess, but likewise completely removes the primary focus of disease. The area of abscess is laid open, when possible, from the primary lesion throughout the whole extent of the disease. The tuberculous granulations are completely removed with Barker's spoon and gauze. Any adjacent areas of bone-disease are firmly curetted and touched with pure carbolic acid. Loose fragments of bone are removed. After irrigation and the arrest of bleeding, the wound is nearly closed, room being left at the most suitable spot for drainage. Dressings, compresses, and bandages are applied. If the entire tuberculous area is thus removed and the raw surfaces are placed in contact with pressure, there is not any more danger of secondary pyogenic infection than there would be in an ordinary wound.

General Treatment.—The general treatment of cold abscess is the general treatment of tuberculosis in any region, and is discussed under the heading of Treatment, on page 630.

DIAGNOSIS OF TUBERCULOSIS.

The existence of an area of intractable chronic inflammation in bone, joint, gland, tendon-sheath—in fact, in any structure—suggests tuberculosis as the cause; and the possibility of this cause must always be carefully considered. The patient's history, habits, occupation, mode of life, etc., must be inquired into; and his tendencies and predispositions, inherited or acquired, must be investigated. Not only must the local disease be carefully studied, but the body at large must be examined. It is necessary to determine whether there is disease, tuberculous or non-tuberculous, in any other locality than the suspected region. The general health must be carefully gaged, and the blood and the urine must be thoroughly studied.

It is often impossible to make the diagnosis of a tuberculous lesion through clinical observation alone. In some cases, in order to make the diagnosis, it becomes necessary to study with the microscope stained specimens of tissue, fluid, or débris that have been obtained from the suspected region. In a doubtful area of chronic thickening, a piece of tissue may be removed with Warren's harpoon, and sections may be made for microscopic study. Fluid for study may be obtained by the use of a tubular exploring needle. Cultures may be taken from fluid, tissue débris, or sections of removed tissue.

It is sometimes desirable to inoculate a guinea-pig with suspected material. Not unusually, when no bacteria have been found with the microscope, and when even the cultures have remained sterile,—which, as before stated, suggests tuberculosis,—the injection of the apparently sterile fluid into a guinea-pig causes the animal to develop miliary tuberculosis in a few weeks. Such an observation demonstrates that the primary lesion has been tuberculous, and also seems to demonstrate that our laboratory methods are still at times so faulty that a fluid supposed to be sterile may actually contain bacteria—as this fluid must have done, if its inoculation has produced the disease.

In suspected tuberculosis of the membranes of the brain, the condition known as tuberculous meningitis, the operation of lumbar puncture should be performed; and the fluid that is obtained should be carefully studied. If tuberculous meningitis exists, and if the exudate has blocked the foramen of Magendie and the foramina of Key and Retzius, then the area of tuberculosis in the membranes of the brain may be cut off from the spinal cord, and the fluid obtained from within the theca of the cord may show no characteristic changes, being perfectly clear and natural-looking; but, as a rule, the cerebrospinal fluid in the subarachnoid space of the cord is present in increased quantity in tuberculous meningitis. It exhibits increased tension on emergence; and is turbid, owing to the presence of pus and white blood-corpuscles. Sometimes blood or fragments of fibrin may be present. Often, but not invariably, the fluid contains the bacilli of tuberculosis. In intra-abdominal tuberculosis an exploratory abdominal incision is sometimes necessary to make the diagnosis clear.

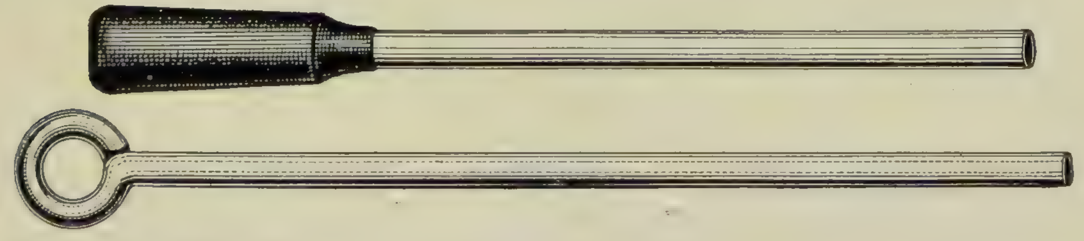


FIG. 161.—WARREN'S HARPOON FOR THE REMOVAL OF TISSUE FROM SOLID TUMORS FOR MICROSCOPIC EXAMINATION.

The x-rays are of very great value in the diagnosis of osseous and articular tuberculosis, and of some considerable value in that of pulmonary lesions. An area of tuberculosis, as exhibited by the x-rays, is much lighter than the surrounding healthy structure.

The Tuberculin Test.—If only moderate quantities of tuberculin are injected, and if the disease is not far advanced, there is very little danger of causing the dissemination of tubercle. For diagnostic purposes, the fluid is given hypodermatically, in a dose of one milligram. If this produces no reaction, the physician waits for from twenty-four to thirty-six hours, and then gives a dose of two milligrams. If this also fails to cause a reaction, he again waits for the same length of time as before, and gives a dose of three milligrams; and so on, until a dose of eight or ten milligrams has been employed. When using tuberculin for diagnostic purposes, the dose of ten milligrams should not be exceeded.

The injection must be made with every aseptic care. The material is mixed with distilled water until it has a tuberculin strength of 10 per cent.; and it is a good plan to have the water contain 2 per cent. of carbolic acid. Norman Bridge says that at the time the administration is made, the above-named fluid should be converted into a 1 per cent. solution by diluting it "ten-fold with distilled water. This represents one milligram of tuberculin in one and one-half minims."[36]

Tuberculin is never given for diagnostic purposes unless the temperature is normal or very nearly so. As Bridge says: "In making the test, the temperature should be taken every two hours for a day before the injection; and as often for a day afterward, in order to be sure of the precise effect of the procedure."[37]

The reaction that occurs in tuberculous subjects has been previously described (page 603). The local reaction at the seat of tuberculosis consists in congestion or inflammation, and the constitutional reaction is indicated by elevated temperature. In tuberculosis of the skin the local reaction can be thoroughly studied. In tuberculosis of joints the skin above these parts reddens. In tuberculous lesions of the oral cavity the surgeon can study the changes that ensue. By means of the laryngoscope, he can study the reaction in tuberculous laryngitis; and by using the cystoscope, he can do so in tuberculous cystitis.

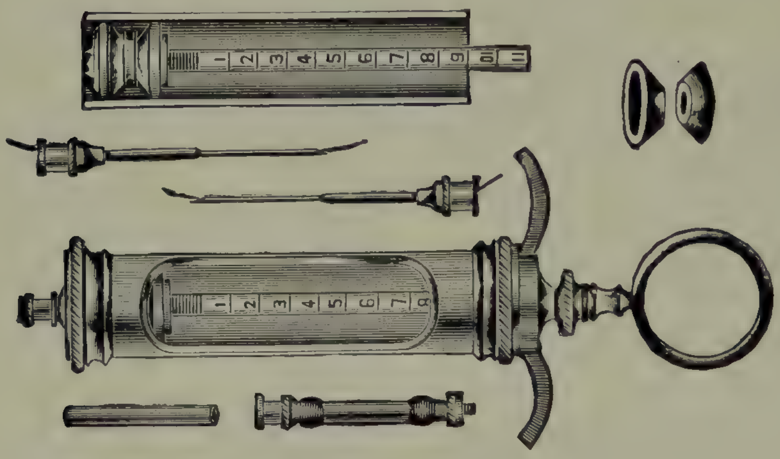


FIG. 162.—ANTITOXIN SYRINGE.

If, after a careful trial of tuberculin, there is no reaction, and if the patient is not in the secondary stage of syphilis, one may usually conclude with reasonable certainty that the patient is not suffering with tuberculosis. In very advanced cases of pulmonary tuberculosis, particularly, there is sometimes no reaction; but in such cases the diagnosis is entirely sure without the test, and there is no use of employing it. A very large dose may occasionally produce a decided reaction in a non-tuberculous individual; but very large doses should not be given. An occasional source of confusion is that a marked reaction is sometimes obtained in secondary syphilis. In tuberculosis of the kidney there are often considerable periods during which no bacilli can be found in the urine; but, as Czerny has shown, the administration of tuberculin will cause quantities of bacilli to appear quickly in the urine. The views of Mérieux and Baillar as to the diagnostic value of injecting blister-fluid from a tuberculous person into a tuberculous animal have been set forth on page 603.

The Agglutination Test.—The blood-serum of a tuberculous subject frequently causes the agglutination of tubercle bacilli; but the test is difficult, requires careful manipulation, and is by no means certain. J. C. Da Costa, Jr.,[38] says: "The serum-test in tuberculosis, as at present elaborated, must be considered of questionable diagnostic value; since it has been shown that it may occur in normal persons and in non-tuberculous diseases, and that it may often be negative in affections undoubtedly tuberculous."

Bacilli in the Blood.—The bacilli of tuberculosis can very seldom be isolated from the blood, even when the lesions are extensive or multiple. Occasionally, however, in the miliary form of the disease, they are found.

PROGNOSIS.

Beyond any doubt, many cases of tuberculosis are cured. This fact is proved by a multitude of clinical observations, and also by numerous necropsies in which healed tuberculous lesions have been found. The different methods by which a tuberculous lesion may heal have already been discussed. When the opsonic index is high the prognosis is far better than when it is low, a high opsonic index indicating that the leukocytes exhibit great phagocytic activity toward the bacilli of tuberculosis

If a tuberculous lesion or if lesions can be removed or sterilized, the prognosis is reasonably good, provided there are not multiple lesions; that the general health is fairly well preserved; that the digestion is not seriously impaired; that there is little anemia; that mixed infection and albuminoid change are not present; and that the patient is able to adopt a hygienic mode of life and to obtain and take a sufficient quantity of nutritious food. The prognosis depends to some extent upon the patient's habits, mode of life, social station, monetary condition, disposition, and temperament. His means may decide whether or not it is possible to treat him in the best way and in the best place; his disposition and temperament tell us whether he will be likely to obey orders, and live by rule and line. The grave dangers of mixed infection and albuminoid change have already been dwelt upon. Albuminoid change is of extremely unfavorable augury; but, as previously stated, some persons apparently recover from tuberculosis in spite of it, although the area that is albuminoid remains so.

The prognosis, of course, varies with the age, the sex, the duration of the condition, the extent of the process, and the situation of the lesion. It is bad in very young children, but is better in older children than in adults; and it seems to be somewhat better in males than in females. Tuberculosis of the skin gives a reasonably good prognosis. Areas of glandular, osseous, and articular tuberculosis frequently heal.

Any tuberculous lesion, however, it matters not how small it may be or how recently it may have appeared, is a profound danger to the entire organism. It is always to be borne in mind that although the disease may be apparently cured, it strongly tends to recur in the same region or near it, or to appear at some later time in another part; and that in many cases in which it seems to be entirely localized, distant and dangerous lesions exist that are undiscovered. It is a well-known fact that when pulmonary phthisis seems to be in a latent state, placing the patient in bed and performing a surgical operation, even upon a part of his body that is distant from the lesion, will frequently cause the disease-process in the lung to wake into virulent activity and spread with dreadful speed. It is my profound belief that the administration of ether or chloroform is sometimes chiefly responsible for the awakening of the area of pulmonary disease. In such subjects an accident may be followed by the rapid development of the process; and in such subjects, only absolutely necessary operations should be performed. If undertaken, the operation should, if possible, be done under a local anesthetic or spinal anesthesia. The operation that can be the most quickly performed and will be followed by the shortest convalescence should be selected; and, at the very first possible moment, the patient should be gotten out into the open air.

TREATMENT OF SURGICAL TUBERCULOSIS.

During the treatment of any tuberculous lesion, the surgeon must always bear in mind the possibility of healthy persons becoming infected from the case. He should, therefore, see to it that any infected excretion or discharge is promptly disinfected; and that materials, such as dressings, coming in contact with the patient are destroyed with fire. These precautions must be taken in every form of tuberculosis, medical and surgical. The basis of treatment is the effort to employ any and all means which tend to raise the opsonic index or, in other words, which tend to strengthen the phagocytic power of leukocytes toward the bacilli of the disease. The value of climate, fresh air, sunlight, food, etc., depends on their power to do this.

In tuberculosis of the lungs, the question of what climate is suitable for the particular case is of great importance. In no region of the earth are people entirely free from the possibility of contracting the disease; hence, there is no place to which a man can be sent that is absolutely fatal to the bacilli. In some climates, however, cases do better than in others; and mere change in itself is often beneficial, by improving the appetite, inducing sleep, and stimulating interest in life and a hope that, perhaps, has long been dormant.

In some cases the limited means of the patient, the advanced stage of the disease, or the existence of certain complications forbids a change being made. In pulmonary tuberculosis all these questions are decided by the physician. If a change is possible, and if the physician considers it desirable, he may send the patient, according to circumstances, to the mountains, to the South, or even, as a few observers have proposed, to some Arctic locality. Osler says that the desirable climatic elements are "pure atmosphere, equable temperature, and maximum amount of sunshine." In most cases of phthisis a mild climate is desirable; as the very mildness lures a person to live much out of doors, and as he thus obtains the benefit that fresh air confers.

In tuberculosis of bones, glands, joints, etc., climate is not nearly so important as it is in tuberculosis of the lungs; but sun and fresh air are of vast importance in any tuberculous condition. It may be considered desirable to send the victim of surgical tuberculosis far away, if his means admit of it; but it is not nearly so necessary to do so as it may be in phthisis. Some patients do very well at home or a little distance off, if proper precautions can be taken to secure an open-air life. Drugs are only accessories. Their importance is entirely secondary. Fresh air, feeding, and the direct rays of the sun are the most potent elements in effecting a cure. It is imperative that the patient shall spend hours a day in the fresh air; and, if it can be arranged, he should sleep at night directly exposed to the air. It is desirable that the air should be free from dust, foul odors, and other impurities. The very poorest patients must attempt to get this fresh air at home, if it is not possible to send them to a camp, a colony, or a sanatorium. Halsted is a believer in the Adirondacks. In the large cities near the ocean many can be sent to the seaside, there to dwell in institutions or tents. Beyond doubt, the sea-air is of the very highest value in surgical tuberculosis; and it is my custom, whenever possible, to send cases to Atlantic City[39] or some other coast resort. The time that such a life should be pursued is a matter of uncertainty in each case; certainly for some months, however, and not improbably for a year or more. We estimate recovery by finding a notable gain in weight, absence of fever, return of function, etc. Halsted points out that even the cured cases exhibit a reaction to tuberculin, hence that tuberculin cannot be used to determine the question of cure.

Frequently an operation is performed in a great city; and, as soon afterward as the patient can safely travel, he is sent to a seaside colony or a sanatorium, where he can obtain the benefits of watchful guidance, fresh air, sunshine, properly regulated exercise, and suitable diet. It would be well if most of these patients could be operated upon at the seaside, and thus obtain the beneficial effects at the earliest possible moment. It is extremely important that they should have watchful care, wherever they go; otherwise, it is improbable that they will live out of doors enough. The widespread public dread of taking cold is ever present in the minds of most persons. Many of them will evade the necessary exposure through fear of harm, laziness, indifference, or a feeling of weariness; or on account of the orders or suggestions of ignorant, although well-meaning, relatives. The world has long recognized the value of fresh air in pulmonary tuberculosis; but we are only just beginning to realize thoroughly its great benefit in all forms of the disease. We are just coming to understand that it is of as much value in tuberculosis of bone, joint, gland, or the peritoneum as it is in tuberculosis of the larynx or the lungs. Many times in children suffering with obstinate tuberculous sinuses have I seen these rapidly heal under the benign influence of the open air, particularly the sea-air. Even when visceral albuminoid changes exist, if they are not too widespread, patients sometimes apparently recover, if taken to the sea-coast; although the albuminoid organ, of course, remains more or less crippled.

The benefit from open air probably depends in large part upon the amount of oxygen it contains. The oxygen, when inhaled, stimulates oxidation, frees the organism from poisons, and favors reparative processes. The benefit also depends in part upon the freedom of the air from poisonous materials—materials that abound in the air of crowded rooms, stores, factories, narrow courts, and jammed street-cars. Close and damp rooms do more harm to tuberculous patients than do northeast storms; and a foul atmosphere is much more injurious than is a March wind. Perhaps the other elements of the air besides oxygen also have a beneficial effect.

Sunshine is of great value in tuberculous conditions. I have already pointed out that it retards the growth of tubercle bacilli. It has been claimed by some observers that the exposure of the skin about a tuberculous joint to the direct rays of the sun is extremely beneficial. The valuable elements are not the heat-rays, and are probably not the light-rays; but are, rather, the chemical rays that exist beyond the violet end of the spectrum. These rays have considerable penetrating power, have a remarkable effect on nutritive processes, and are somewhat germicidal. Finsen has utilized the power of the chemical rays to cure surface-tuberculosis, especially lupus. A victim of tuberculous disease should be as much as possible in the sunlight, except in torrid weather.

The seat of tuberculous disease requires rest. Confinement in a poorly ventilated room, and particularly confinement to bed in such a room, may, however, be most disastrous, and may, perhaps, lead to the rapid progress of the disease. The surgeon seems to be forced to choose between the two horns of the dilemma. Certain tuberculous conditions of the peritoneum, of bones, and of joints require confinement to bed; and yet, confinement to bed may make the patient worse, or may actually kill him. The confinement that makes him worse is not, however, the judicious, but the injudicious confinement. For instance, a tuberculous patient with fever should remain in bed; because exercise increases fever. Exercise is often most injudiciously insisted upon; and even when a patient is free from fever, exercise should not be indulged in to the point of tiring. It is obvious that confinement to bed may be necessary, but this direction does not mean confinement in a close room. Confinement in an ill-ventilated room causes loss of appetite, weakness, anemia, and lowered vital resistance. As a consequence, the initial tuberculous focus spreads, and new foci may develop in near or distant parts.

Surgeons long ago discovered that these evil results of confinement to bed are greatly mitigated, or even abolished, if the room is very well ventilated. At the present time we know that, whenever indicated, rest in bed may be insisted upon without any fear of ill results, if there is a plentiful supply of fresh air. The patient is kept warmly covered;

a skull-cap is placed on his head; and the freest ingress of fresh air, but without draught, is permitted. A victim of surgical tuberculosis who must be confined to bed is often best cared for in a tent or cottage-sanatorium; or, perhaps, a porch that has been altered for the purpose may be used. In the Johns Hopkins Hospital the "bridge" from the wards to the clinics is used for this purpose.

At the first moment consistent with safety the patient is got out of doors, retentive apparatus being applied, in many cases, to secure continued rest to the diseased part. A drawback to hospital treatment in great cities, as applied to many tuberculous conditions, is that few institutions have the proper facilities for the fresh-air treatment; and that the necessity of caring for other patients as well as the tuberculous has to be considered.

It will be seen from the preceding remarks that the necessities for treating surgical tuberculosis are physiologic rest and plenty of fresh air.[40] As Burrell [41] says: "The prime essentials in the treatment of tuberculosis are physiologic rest, outdoor treatment, and ample nutrition of the patient. Whether the tuberculous area is in the lung, in a joint, in a lymph node or in the intestine is a detail." Confinement to bed is practised only in complicated, advanced, or febrile cases. When employed, the greatest care is taken to secure a fresh ingress of air; and the bed is abandoned at the first safe moment. Dr. H. Augustus Wilson [42] says: "The advocacy of locally applied restraint, and freedom for the rest of the body, deprecates confinement to bed, or even within doors."

In the very nature of things, most operations for surgical tuberculosis are done in the large cities; but, as soon as the patient becomes convalescent and it is regarded as safe to move him, and if his circumstances permit of it, he is taken to a camp or a sanatorium in the mountains or the country, or at the seaside. Thus will vital resistance be greatly invigorated, and the tendency to permanent cure vastly strengthened.* As Dr. H. Augustus Wilson says in his previously quoted paper:[42] "The best results are to be secured by having the patient out of doors all the daylight hours, and sleeping with the windows wide open or in tents. In stormy weather porches or other suitable shelters will protect the patient against unnecessary exposure. Ample warm clothing and the resort to such activity as the peculiar conditions of the patients warrant will enable them to keep warm. Usually, the appetite begins to improve within a day or two; and this enables the patient to accept largely of nourishing food—eggs, milk, and cream forming the principal basis." As Dr. Wilson further points out, every city hospital, if it possesses a lawn, should have tents for tuberculous patients; or it should utilize verandas or the roof for this purpose. At least seventeen years ago Professor Halsted, of Baltimore, advocated the treatment of all cases of tuberculosis "irrespective of the situation of the lesion" by life in the open air; and he believes that "most cases of surgical tuberculosis will recover without operation if they are given a fair opportunity in the open air."[43]

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*Dr. John D. Adams has described the Convalescent Home at Wellesley Hills, Massachusetts. In this institution, during both summer and winter, tuberculous children live and sleep in little shacks, so open that the occupant is practically out of doors.

Baths.—There are two disagreeable varieties of patients: One class is composed of the individuals that feel it a religious duty to wash with painful frequency; and the other, those that never wash at all. It is difficult to say which class gives one the most trouble. In tuberculous cases, when the condition of the patient admits of it, a daily bath is desirable. It may consist of tepid water or even a cold spray, if the patient reacts well from it; and it should be followed by rubbing with alcohol and frictions with a coarse towel. If the individual is confined to bed and in a febrile state, the nurse should wash him each day in the same manner as she washes any other febrile patient. It is quite clear that persons that are weak and exhausted, and do not react well, should not take a general bath; and, particularly, that they should not take a cold spray or a cold bath. Such persons must remain satisfied with a sponge-bath and an alcohol rub.

Exercise and Massage.—I have already dwelt upon the fact that persons with fever must not exercise, but must be in bed; and that no tuberculous patient must exercise to the point of being fatigued. Short of this, exercise is very beneficial. The value of the alcohol-rub and of frictions with a towel after a bath has been referred to. If the patient takes but a small amount of exercise, massage may be desirable; and it probably aids the nutrition of the body. Under no circumstances, however, should it be applied to the region of tuberculosis; although in some cases it is permissible lightly to rub certain drugs (iodoform or guaiacol) into the skin over the tuberculous area. A tendon should remain quiet if in a tuberculous sheath; a tuberculous joint should be immobilized; a tuberculous gland, a tuberculous bone, and a tuberculous abscess should be guarded from manipulation. Massage, if applied to a tuberculous area, may disseminate the disease.

Diet.—It is desirable that a tuberculous patient should consume and digest more food than will suffice to supply waste; in other words, it is desirable that he should be overfed. He should not be fed exclusively, or even very largely, on a single article of food. The diet should be mixed, and should contain a sufficiency, not only of fats and proteids, but also of carbohydrates. The necessary mixture of nutritive elements should be in an assimilable form. In many cases of tuberculosis the appetite is destroyed; and in most, it is at least impaired and capricious. Unpalatable materials excite disgust, inhibit the taking of sufficient food, and impair digestion.

There is no such thing as a diet-cure for tuberculosis, although many alleged diet-cures have been and are employed. There is no plan of diet that is capable of exerting a specific influence upon the disease. Diet is serviceable in proportion to the amount of nutritive material consumed and digested; and it acts purely by improving the health, the strength, and the body resistance. There are many alleged specific diets, such as the grape-cure, the whey-cure, the milk-cure, the blood-cure, etc.; but what has just been said applies to them all.

Every care must be taken to save the patient from indigestion, as this would cause him to take insufficient and probably improper food. Dyspepsia often arises through the taking of too great an amount of food at a single meal. Such an excess is by no means uncommon, when an individual has been profoundly impressed with the necessity of taking ample nourishment and is conscientiously trying to obey orders. It is wiser to take smaller amounts at frequent intervals than to overeat three times a day. The patient, when awake, should take food every four hours; and its nature and amount should be adjusted, as far as possible, not only to the nutritive demands of the tissues, but also to the capacity of the stomach and the longings of the appetite. If there is any failure in digestion or any difficulty with the bowels, ordinary medical means should at once be employed to amend the trouble.

Milk is a very valuable food. Most persons are able to take it raw; but some can take it only when it is mixed with other articles, such as lime-water or a little sodium bicarbonate and sodium chlorid. Milk with hot water or milk with brandy is palatable. Children should not have boiled milk exclusively given them, as such a diet may occasionally be followed by scurvy. Many persons claim that they cannot take milk, but find that they can when compelled to try. Even those whom a glassful of raw milk makes bilious can take the fluid in smaller quantities; or can even digest a full glass, if crackers are crumbled into the fluid and the mixture is eaten with a spoon. If milk causes constipation, a sufficient amount of the fluid extract of cascara sagrada to correct this tendency should be taken at night.

Eggs are also useful. They are preferably given very soft-boiled, or perhaps in milk, or as one of the constituents of egg-nog. If the condition of the patient admits of the use of solid food, meat, particularly underdone meat, is always used. Raw beef is very useful, given in the form of meat pulp—the meat being scraped, ground, and sieved; seasoned to taste; and eaten with a little dry bread. Bread is given as toast or stale bread; and it should be eaten with plenty of good butter, which is a palatable fat of high nutritive value. Many tuberculous patients abhor ordinary fat, and one may have great difficulty in persuading them to eat fat meat; but they will take butter and like it, and crackers and butter are palatable to many. Whenever solid food is being taken, vegetables and fruits, especially grapes, should constitute a part of the diet. If children do not have vegetables or fruit given them, they may develop scurvy. The foods above recommended may be given in various forms and combinations, and from them a reasonably varied diet-scale may be constructed.

Cod-liver oil is a valuable fat, if the patient can take it; but some patients cannot, and others will not. If used at all, it should be pure, the light-yellow oil being the proper form. The brown oil should never be employed. The nutritive value of emulsions is probably not high. Capsules may be unreliable, owing to insolubility. Some think that the value of cod-liver oil depends purely on the fact that it is a fat; others believe that it contains elements that have a positive influence in antagonizing tuberculosis and in promoting constructive metamorphosis. The former view is probably the correct one. As a rule, inordinately large doses are given. They excite disgust, and cannot be assimilated; because disgust not only destroys appetite, but impairs digestion. The surplus oil appears in the stools as free oil. The judicious dose for an adult is a teaspoonful. It should not be given immediately after meals, but two or three hours afterward—a period at which intestinal digestion is going on; the oil being digested in the intestine, and not in the stomach. If three doses a day excite disgust, give a single dose of three teaspoonfuls at bedtime. The proper dose for a child is thirty drops three times a day; and for an infant, ten to fifteen drops three times a day. Young children rarely object to taking the oil, and often actually grow fond of it. Cod-liver oil should not be given if fever exists, if the digestion is greatly impaired, or if the material causes diarrhea or excites genuine disgust. Neither should it be given during the hot summer months, because it is then liable to cause diarrhea.

The Specific Treatment.—The specific treatment with serums and with tuberculin has utterly failed to realize the high expectation at one time entertained concerning it. The antitoxin made by injecting a number of doses of tuberculin into a horse and obtaining blood-serum from the supposedly immune animal has not produced any notably good results. Tuberculin itself seems very unreliable, and the results from its use are by no means certainly good. As set forth under the heading of Diagnosis, we know that the ordinary dose of one milligram may produce fever in the tuberculous; but, when used in treating the disease, the tuberculin is given in such small doses that it does not produce fever. As Bridge[44] points out, the injection is repeated every few days; and after a number of injections the patient develops a considerable degree of tolerance, when the dose may be increased. The tuberculin treatment is never attempted if the disease is far advanced or if there is mixed infection with pyogenic organisms. The one form of tuberculosis in which tuberculin has occasionally produced definitely valuable results is lupus.

Treatment by the Administration of Drugs.—Many drugs have been highly lauded; but there is none, except perhaps tuberculin, that is specifically antituberculous when given internally. Many drugs, however, are given with this aim: among them are beechwood creosote, guaiacol carbonate, arsenious acid, and alcohol. Iodoform inunctions and painting the surface with guaiacol have been advocated.

Alcohol is often useful in tuberculosis. To say that a man has this disease is not equivalent to saying, as many of the laity seem to think, that alcohol is required. As a matter of fact, however, tuberculous subjects are wonderfully tolerant to alcohol; but this does not prove that the drug is needed. Many patients do without it entirely, and it is better avoided in children, unless there is a particular indication for its use. Usually it is advisable, when a patient is weak or exhausted, to give milk-punch or egg-nog. In all conditions of exhaustion, particularly in mixed infection, alcohol is needed; and when needed, it should be given in full physiologic doses. If, in a patient with fever, alcohol increases the pulse, makes the delirium worse, and flushes the face, its amount should be diminished or its use should be discontinued. If the patient smells strongly of it, he is taking too much. Alcohol is often of much service if there is chronic dyspepsia.

Tonics are very useful in tuberculosis. The syrup of the iodid of iron is particularly valuable in children. A mixture of iron, quinin, and strychnin, in combination; and arsenic, given alone or with iron and strychnin, are especially serviceable in adults.

Remedies may be needed to improve the digestion and combat diarrhea, or to prevent constipation. Malt has been warmly advocated by some as a valuable material to aid in the digestion of starches. I have never become convinced that the nucleins are productive of any benefit. Among the remedies that are sometimes of value may be mentioned Fowler's solution of arsenic and the hypophosphites. Sweats, cough, sleeplessness, pain, etc., may be treated by the ordinary drugs and methods.

Local Treatment of Tuberculosis.—Many drugs, when locally applied, have more or less antituberculous power. At the head of the list stands iodoform; and then come guaiacol, balsam of Peru, and chlorid of zinc. Iodoform is most powerful when acting in a region free from air, as when it is injected into the cavity of a tuberculous abscess. Guaiacol is thought by some to be valuable when rubbed into the skin over a tuberculous gland or a tuberculous tendon-sheath, but I have never been satisfied that it does good. Chlorid of zinc, when injected about a tuberculous lesion, may cause the formation of quantities of fibrous tissue, which will perhaps encompass the lesion and eventually destroy it. Lannelongue is a warm advocate of chlorid of zinc, and Landerer advocates balsam of Peru in some cases and cinnamic acid in others. Oil of cinnamon is used locally by some. Ichthyol in lanolin is used by some to rub into the skin over recent tuberculous glands, tendons, or joints; and blue ointment, when applied locally, is frequently of benefit in lupus. Camphorated naphthol is used to inject tuberculous nodules, and it is introduced by means of a hypodermatic needle.

Whatever drug is applied to the tuberculous focus, or however it acts, that region requires rest; and in many cases the rest is given by the application of a splint or by orthopedic apparatus.

Operative Treatment and Special Methods.—The principles involved in the surgical treatment are to empty and remove any tuberculous foci and to destroy the bacilli that are present. An accessible area may be attacked, and the infected tissue may be removed. Such radical intervention is not always necessary, however; and, in certain abscesses, we can only in part carry out the rule. Nevertheless, it is extremely undesirable and often dangerous to remove but a part of a disease-focus. Incomplete operations are frequently followed by a diffusion of the disease, because the operation opens up pathways of absorption that have previously been blocked by white blood-corpuscles or fibrous tissue. The methods of surgical treatment applied to particular forms of the disease will be referred to in the subsequent pages of this chapter and will be dwelt upon at length in other portions of the work.

Bier's Method of Treatment.[45]—Bier advocates, under certain circumstances, the production of active or passive hyperemia in an inflamed area. Active hyperemia is obtained by heat and is especially useful in causing the absorption of the products of a chronic inflammation. It is not so useful in an acute inflammation as is passive hyperemia. In tuberculous conditions, especially in tuberculosis of the bones and joints, Bier finds passive hyperemia of the greatest curative value. He obtains it in some parts by compression of the veins coming from the part, and in others by means of special cupping-vessels or jars. The vacuum cups are shaped to fit particular parts. The air in the cup is exhausted by a bulb or pump. In tuberculous abscess upon the body he makes a small incision with aseptic care, and applies a vacuum cup for three-quarters of an hour a day. He thus combines evaporation and hyperemia. In an extremity he obtains hyperemia by applying a Martin rubber band above the area, putting it on with sufficient tightness to interfere with venous return from the part, but not with sufficient tightness to block the arterial stream, or to cause pain, swelling, or coldness. Originally, his purpose was to get the patients so used to the band that they could wear it day and night; but he has abandoned this idea, and now believes that it is sufficient to apply it for two or three hours a day. As a matter of fact, passive congestion may be produced as well with an ordinary bandage as with the rubber band. In treating a tuberculous part Bier does not use splints but depends on hyperemia. He does not inject iodoform unless the part contains serum or pus, and even if he does use iodoform he also uses the band.

The method is undoubtedly of value in some cases; it is frequently of great value, and may produce a cure in an obstinate tuberculous lesion. It certainly lessens pain in an area of inflammation. It must be used with caution, as its limitations are still somewhat ill defined. The degree of hyperemia must be moderate, and must never be sufficient to result in pain, in white edematous swelling, in coldness or anesthesia of the part; and the constriction or suction must never be protracted beyond a very few hours. The method is applied particularly in tuberculosis of the joints. In tuberculosis of the knee-joint the bandage is placed on the upper part of the limb, close above the knee, just tight enough to cause congestion. Then a flannel bandage is applied from the toes to the lower border of the knee, there being thus produced an area of congestion limited to the area of disease. The bandage is kept in place one, two, or several hours. It is then removed, to be reapplied the next day; and so on. In the intervals between the applications the part should be at rest.

The treatment is founded upon the principle announced by Laënnec many years ago, that cyanosis is antagonistic to tubercle. Exactly why Bier's congestive hyperemia should cure tuberculosis has been much discussed. It certainly increases the exudation of blood liquor and the migration of leukocytes. Nötzel, quoted by Bier in his recent book,[45] states that the healing influence is due to the increased bactericidal properties of the blood when it is thus imprisoned. Buchner thinks that it is due to an increase in the number of leukocytes. Heller, who is also quoted by Bier in his book, states that the bandage acts by holding back the toxins. Richter believes that the disturbance of the circulation leads to the migration of quantities of leukocytes. Hamberger is of the opinion that it increases the amount of bactericidal blood-serum in the part. Bier, after having reviewed all these theories, comes to the conclusion that the curative effects probably depend upon phagocytosis. It would seem quite probable that in the area of passive congestion the tissue-cells might form antitoxins that would attenuate the virulence of the tuberculous virus.

The Finsen Light.—The late Dr. Finsen, of Copenhagen, proved that the powerful chemical rays of the sunlight have positive germicidal power; and that, if these rays are concentrated by certain special apparatus, their germicidal power is notably increased. He further showed that vast numbers of chemical rays can be obtained from the electric light. He applied these rays, having first used the rays of the sun, and later the actinic rays from electric light, for the treatment of local areas of tuberculosis. Beyond any doubt, they are capable of producing cure. They are most useful in lupus; but, to be successful, they must be applied for many weeks or months.

The X-Rays.—The x-rays are also used in the treatment of certain areas of local tuberculosis, but are particularly serviceable in treating lupus, over which they seem to exercise almost as favorable an influence as do the actinic rays; and the effects are much more rapid.

TUBERCULOSIS OF THE SKIN.*

Tuberculosis of the skin may present itself in many forms, which are, after all, but manifestations of different stages of the tuberculous process. Cutaneous tuberculosis is apt to occur in persons who already suffer from a tuberculous lesion, or in those that are predisposed to tuberculosis by heredity; but it may arise in individuals entirely free from other tuberculous lesions, and without any apparent predisposition. It is seen most usually, however, in tuberculous families, and is particularly common in those that dwell with the tuberculous. In some cases it is due to direct inoculation with human or bovine bacilli; in some, it is secondary to mucous lesions; in some, it is but a part of a general miliary tuberculosis.

Stelwagon[46] includes all the various manifestations of skin-tuberculosis under five headings, viz.: (1) Ulcerating tuberculosis; (2) disseminated tuberculosis; (3) warty tuberculosis; (4) scrofulodermata; (5) lupus vulgaris.

1. Ulcerating Tuberculosis (Tuberculosis Ulcerosa, Miliary Tuberculosis of the Skin, Tuberculosis of the True Skin).—This form of cutaneous tuberculosis appears about the orifices of mucous canals, such as the nostrils, the lips, the anus, the vagina, and the urethra. It is usually due to inoculation with the discharge from a preëxisting area of mucous tuberculosis, or to the direct extension of such an area to the skin; although, according to Ehrmann,[47] inoculation from without is occasionally responsible for the condition. This observer states that the saliva of a tuberculous individual conducting ritual circumcision may cause the disease to appear upon the foreskin, glans, or meatus of the subject operated upon. That the fluids coming from the tuberculous area may convey the bacilli to a distance and lead to the production of ulcerating tuberculosis of the skin is proved by cases in which tuberculosis of the kidney has been followed by tuberculosis of the head of the penis. In some cases, one, several, or all the intervening structures—the bladder, the prostate, the seminal vesicles, the urethra—suffer; in others, they remain free. Sometimes, in ulcerating tuberculosis, the bacteria seem to have reached the skin by way of the blood or the lymph, rather than in the usual manner, which is in fluid that bathes the free surface, the bacteria being rubbed into the skin or entering into a crack, an abrasion, or a gland orifice.

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* See also chapter on the Skin.

The form of tuberculosis now under discussion rarely appears, except in exhausted and anemic individuals suffering from advanced tuberculous lesions. It begins with an outbreak of miliary tuberculosis on the cutaneous surface, near the orifice of a mucous canal. The tubercles quickly caseate, and an ulcer or several ulcers, that have no disposition to heal, but spread and run together, are formed. The ulcers met with in this form of tuberculosis are usually free from pain; are irregular, and often serpiginous, in outline; and are crusted at the edges, the edges being non-indurated, livid, and sometimes undermined. When the crust is removed, the floor of such an ulcer is seen to be covered with pale or yellowish granulations, which are often of large size and edematous. The clinical diagnosis is made by the advanced cachexia, the finding of a mucous lesion, the appearance and mode of onset of the ulcers, and the fact that the discharge from these ulcers usually contains numerous bacilli.

Treatment.—The general constitutional treatment is the same as has been set forth in a previous section (page 630). Locally, in some cases, the area is curetted, cauterized with pure carbolic acid, and dressed with iodoform gauze. In other cases the ulcer is cauterized with a solid stick of nitrate of silver, is washed several times a day with hydrogen peroxid, and is dressed with iodoform gauze.

2. Disseminated Tuberculosis (Tuberculosis disseminata).—This is a very unusual condition, and seems to occur only in children—and in children that already suffer with some tuberculous condition, such as pulmonary, osseous, articular, or peritoneal tuberculosis, or tuberculous abscess. It is acute in onset, widespread in distribution, and extremely intractable to treatment; but some few patients do recover. One type is entirely papular; another is polymorphic, exhibiting spots, papules, vesicles, pustules, and crusted ulcers. In disseminated tuberculosis the associated lymphatic glands are usually found to be enlarged. A type of disseminated tuberculosis occasionally follows exanthematous fevers; and presents, as Dr. Stelwagon [48] points out, "a rough resemblance to flat lupus-tubercles, to sluggish acne-papules, and to lichen scrofulosum."

Treatment.—The constitutional treatment is that employed in any tuberculous condition. Locally, it may be advisable to curette the area and dress it with iodoform, or simply to apply iodoform ointment or an ointment containing salicylic acid. In any case, the diseased area should be cleansed daily with hydrogen peroxid, followed by warm normal salt solution.

3. Warty Tuberculosis (Tuberculosis verrucosa).—The form of warty tuberculosis most usually encountered is the anatomic tubercle, or verruca necrogenica, which was first described by Wilkes. It is most liable to be found on a finger, the hand, or the forearm. It may occur in butchers, handlers of hides, nurses, hospital-orderlies, physicians, and those that make post-mortem examinations—in fact, in any one exposed, by his calling or habits, to inoculation with tubercle bacilli. I have seen one case on the knuckle of a man that had cut that part on the teeth of another man during a fight. I have already referred to a case of what was apparently inoculation-tuberculosis, occurring in an attendant of a lunatic-asylum, whose arm had been bitten by a tuberculous patient.

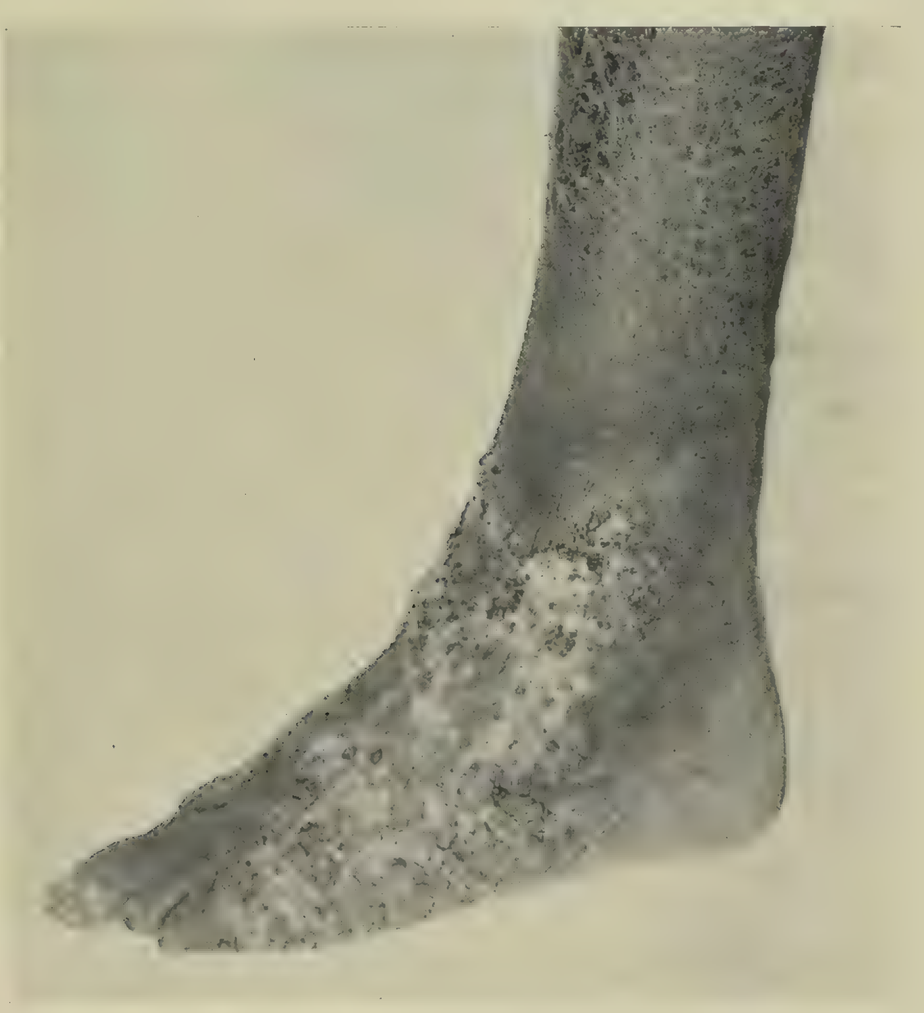

FIG. 163.—TUBERCULOSIS VERRUCOSA CUTIS (Stelwagon).

The anatomic tubercle is produced by direct inoculation with tubercle bacilli. In some cases it begins as a small papule, which may become a pustule, which breaks, and exposes a crusted, papillomatous area, which slowly increases in size and is slightly elevated. In other cases the anatomic tubercle begins as a warty growth, which, when it has attained full size, looks like a group of inflamed warts. The papillomatous or warty surface of an anatomic tubercle is dark red, and the skin about its margin is often purple. The most common size is that of a ten-cent piece, and it seldom becomes larger in diameter than a twenty-five-cent piece. There is slight induration of the edge, a condition that is absent in most other tuberculous lesions.

The anatomic tubercle is slow in progress. It will grow steadily for a time, and then remain stationary—perhaps for months. If no active treatment is instituted, the condition may remain for years. Some few cases, however, undergo spontaneous cure. Sometimes a portion of the tubercle becomes covered with healthy skin, while the disease-process still spreads in another portion. In some cases the disease remains local; in others, the bacilli pass up in the lymph-stream to the lymph glands. The lymphatic tuberculosis may not get beyond these glands, but it may become widely disseminated.

Another form of warty tuberculosis—due to inoculation, as is the anatomic tubercle—is *tuberculosis verrucosa acutus*. In the beginning it exactly resembles anatomic tubercle in appearance; although there may be two or several points of disease, which afterward coalesce and form a slightly elevated area, of warty appearance and irregular outline. A warty area produced by such coalescence may be four or five times as large as an anatomic tubercle. There may be papules or pustules on the edges of such an area; or pustules may arise among the papillomatous projections, and crusts may form. In some cases a growth that resembles a fungus takes place. Tuberculosis verrucosa acutus pursues the same course as does anatomic tubercle.

The clinical diagnosis of warty tuberculosis due to inoculation is made by the extremely chronic course, the dark-red skin, and the fact that general ulceration is not present and that the margin sometimes shows distinct induration. The papillomatous tissue contains tubercle bacilli.

Treatment.—The area should be thoroughly curetted and cauterized with pure carbolic acid; or else extirpated with a knife, the wound being closed with sutures. After curettement or extirpation, dressings of iodoform gauze should be applied, and the part should be put at rest on a splint. In some cases the x-rays or the Finsen light may be preferred to the knife or the curette; but they should rather be supplementary than constitute the sole treatment. Tuberculous glands should be removed surgically. The general treatment of tuberculosis should, of course, be employed; and it should be most rigidly employed, if there is any disposition to lymphatic or constitutional infection.

4. The Scrofulodermata.—When subcutaneous tuberculous lesions caseate and adhere to the skin, the skin becomes discolored, diseased, and thinned, and finally ruptures. Ulcers form, and these ulcers are known as scrofulodermata. In most instances the original lesion is a tuberculous lymph gland; in some, it is a small subcutaneous tuberculous abscess, which is known as *tuberculous gumma.* When such a tuberculous gland softens and adheres to the skin, the skin becomes thin and purple; and if the process advances, as it usually does, the skin gives way at one or several points, and a secondary pyogenic infection takes place in the tuberculous area—if this has not already occurred. If a probe is introduced through one of the openings, it will touch the remains of the diseased gland. Each opening is at first small, but gradually enlarges until it perhaps attains the size of a ten-cent piece, or even that of a twenty-five-cent piece, and two or more openings may run together. A large, characteristic, tuberculous ulcer, surrounded by discolored and diseased skin, forms. In the majority of cases such an ulcer is superficial and spreads at the margin, but rarely deepens. The floor is pale, and possesses no granulation at all; or, which is more common, is covered with large, pale, edematous granulations. In some instances a partly destroyed gland is, or the remains of a gland-capsule are, distinctly visible. The edges of the ulcer are purple and tender; are markedly undermined for a considerable distance; and are very prone to slough. The discharge is thin and scanty, and may or may not contain tubercle bacilli.

A few ulcers heal spontaneously after suppuration has completely destroyed the gland; but a puckered and livid scar, which is a great deformity, results from spontaneous healing. Ulcers may heal in part, but not completely. In a very few cases lupus develops in the skin of the margin. Most ulcers remain open indefinitely and slowly spread, unless active treatment is adopted. The diagnosis of the scrofulodermata depends upon the origin, appearance, and course of the ulceration.

Treatment.—The surgeon should remove the gland with the curette; or, if there are surrounding enlarged glands requiring extirpation, he may remove the whole mass with the knife and the scissors. The diseased and undermined skin must be cut away, as has been directed in the section on tuberculous abscess. The wound may be left open or may be partly closed with stitches; but ample drainage is always provided for by means of iodoform gauze, and constitutional treatment is of the first importance.

5. Lupus Vulgaris.—This disease of the skin or the mucous membrane is produced by the lodgment and the multiplication of the bacilli of tuberculosis in the corium. Papules or nodules of granulomatous tissue form, ulceration occurs, and a scar usually results. The process, as a rule, begins at several limited points; papules forming about the lymph spaces, and channels in the deep portions of the corium. Within the granulation tissue of the papules the bacilli are found. Slow coagulation necrosis takes place in the papules, and new papules are forming while the older ones are undergoing change. A considerable collection of these papules constitutes a patch. During the destruction effected by coagulation necrosis some of the epithelioid cells may proliferate and form connective tissue; and it is common to see scar-formation going on at one part of the patch, while destruction from coagulation necrosis is taking place in other parts. The coagulation necrosis leads to destruction of the skin; and, as the result of this process and secondary pyogenic infection, an ulcer forms.

Occasionally the ulcer heals spontaneously. More often it extends, frequently coming to cover an enormous area. When it extends it does so slowly but inexorably, and becomes hideously destructive. The scar on the healed portion of an ulcer or the scar of an entirely healed ulcer is usually rough, pigmented, and ridged, showing white lines of atrophy. Many of these scars strongly resemble keloid. They are said by Unna to contain no elastic fiber, as do ordinary scars; and also to differ from the latter in the arrangement of the bundles of connective tissue. I have come to regard keloid as probably expressive of an existing or antecedent tuberculous lesion, near or distant. It is not that keloid contains tubercle bacilli, but that it may arise because of the action of the toxins of tubercle bacilli. Studies are now in progress to prove or disprove this view of keloid. Very few tubercle bacilli can be found in the granulation tissue of lupus, and sometimes it is impossible to find any there, those that have once been present having been destroyed.

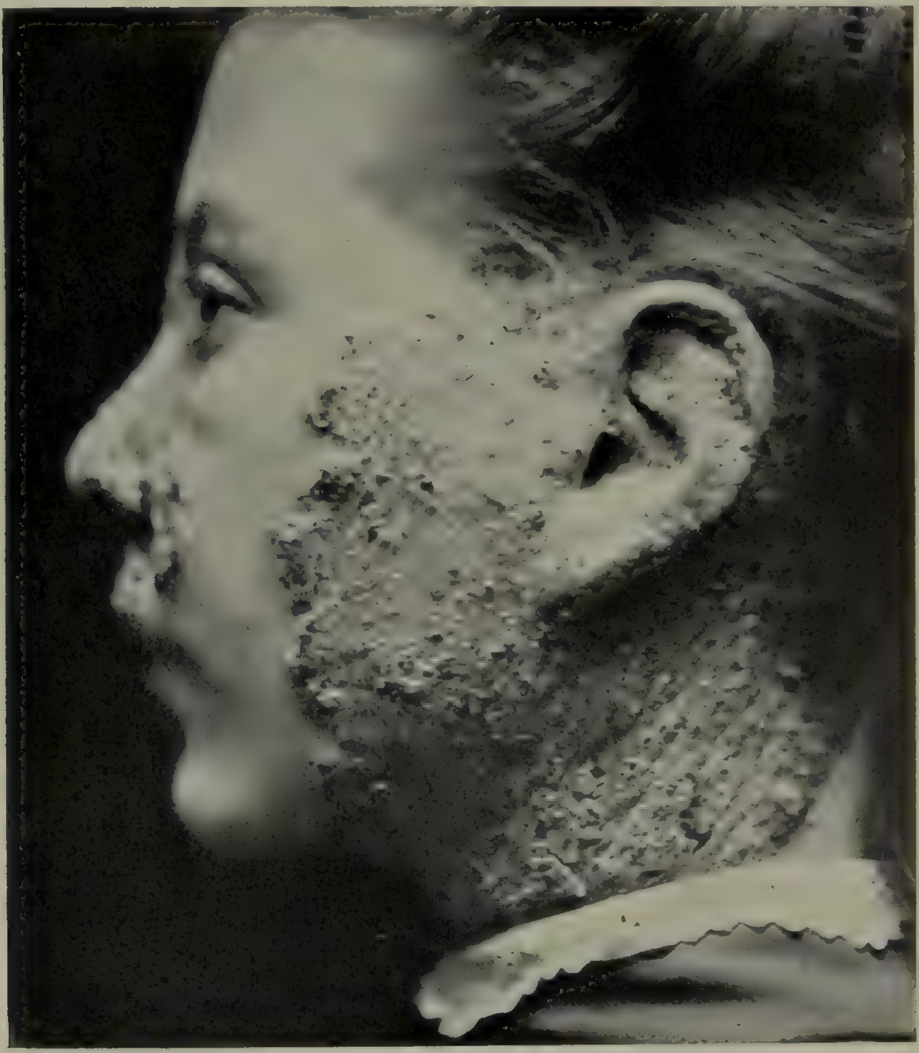

Fig. 164.—Lupus Vulgaris—Tuberculosis Cutis (Stelwagon).

In America lupus is certainly rare; although, now and then, it is met with, being most common among the foreign residents of our great cities. It is far more common in Germany, Denmark, Austria, and France than in England; and is more common in England than in the United States. Stelwagon says that it is quite common in Australia. It is met with two or three times as frequently in women as in men. It is seldom seen before the age of three, it rarely begins after that of twenty, and it is most frequently encountered in subjects between the ages of eight and eighteen. It is not unusual to see an area of healed lupus that has been active in youth break down afresh in adult life; but it is very unusual to find the disease first appearing in adult life, although now and then one meets with such a case.

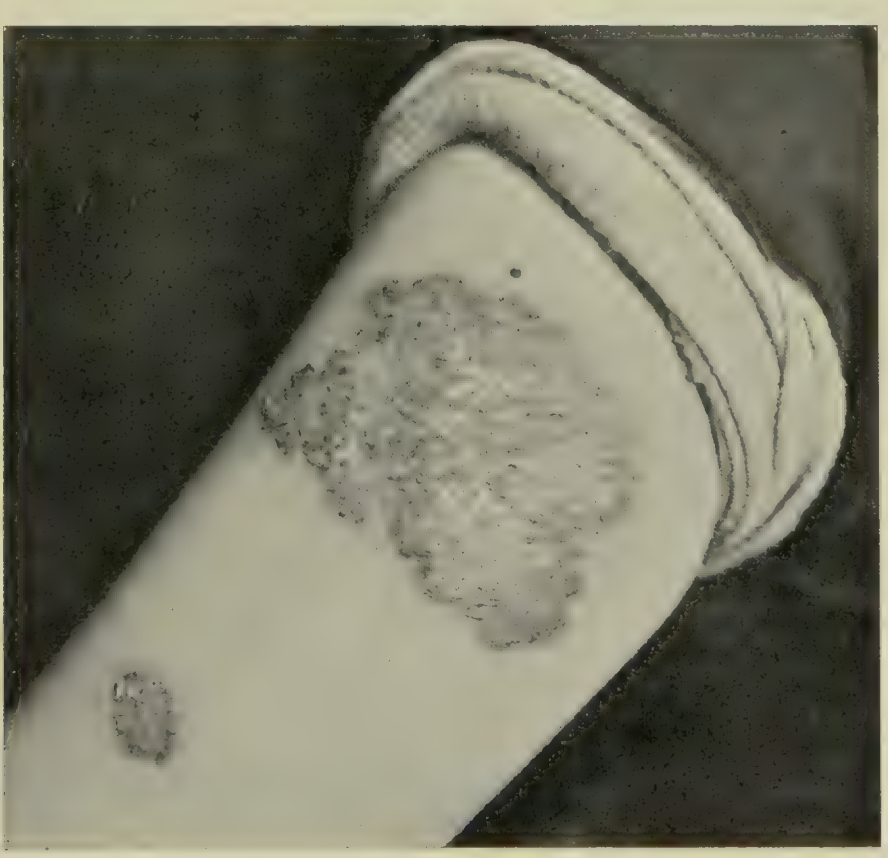

FIG. 165.—LUPUS VULGARIS, FOLLOWING VACCINATION. TUBERCULOSIS CUTIS (Stelwagon).

In about 90 per cent. of the cases the victims of lupus are those predisposed to tuberculosis. It is particularly apt to occur in some person in a family of which one or more members are at that time tuberculous, or in persons who have or have had other tuberculous lesions. Many cases of lupus are followed by the gradual development of a very slow form of pulmonary tuberculosis. Some cases of lupus are due to direct inoculation. One region, or perhaps several, may be affected, simultaneously or consecutively. The region most commonly affected is the face, especially on or about the nose; but the disease may spread on the cheek, the lip, the ear, an extremity, or the genital organs. Primary lupus of a mucous membrane is uncommon, but does occur. Lupus of a mucous membrane adjacent to an area of cutaneous disease is not rare.

Lupus begins as a slowly developing patch of soft nodules, each about the size of a pin's head or somewhat larger, deep in the skin. The color is yellowish or reddish-brown, which pales, but does not completely disappear, on pressure. Gradually new nodules form, and the older nodules undergo degenerative changes. Finally, several or many small ulcers appear.

The lupoid ulcer is very shallow and of rounded outline, and its edges are neither distinctly undermined nor markedly indurated. The discharge is scanty and purulent and forms crusts, and few or no bacilli are found in it. After a time some of the ulcers cicatrize, very dense and glistening scar tissue forming. As the scar is forming at one part of the margin, the patch of lupus is spreading at another part, by the formation of new nodules. Smaller ulcers may coalesce and form large ulcers.

The disease lasts for years. It is very seldom that spontaneous healing occurs. Usually the area slowly but certainly enlarges; although at times, for weeks or months, it may seem to be stationary, it inevitably begins again its march. In some cases adjacent glands enlarge; in others, they are free. In some instances other tuberculous lesions of the skin develop; in others, distant tuberculous lesions arise. The area is rarely painful, unless there is severe secondary pyogenic infection. Lupus, if unchecked, will produce horrible destruction and will eventually cause hideous deformity and death.

Lupus of a mucous membrane may appear as a patch of nodules, or as a group of opacities or ulcerations. When lupus of the skin is accompanied with marked ulceration, the condition is called *lupus exedens.* If the lupoid ulcer assumes a warty appearance, the condition is known as *lupus verrucosa;* if it assumes a papillomatous aspect, it is called *lupus papillomatosus.* If the ulcer becomes serpiginous, the condition is denominated *lupus serpiginosus.* In some cases of lupus ulceration does not occur, but there is fatty degeneration and absorption. A thin, glistening, pigmented scar results. Such a case is called *lupus exfoliativus.* In *lupus hypertrophicus* masses of exuberant granulation arise from the ulcers. There is much inflammation and infiltration about the ulcers, and a very thick and distorted cicatrix results. The scar from any healed area of lupus may be hypertrophied and hard, the condition being known as *lupus sclerosus.* Genuine keloid may develop in the scar tissue. As previously stated, it seems probable that keloid may result from a near-by or distant lesion of tuberculosis, the toxins of tuberculosis causing the production of the characteristic cicatrix. It is by no means certain that the disease known as *lupus erythematosus* is connected with tuberculosis. Bacilli are certainly not found in the lesion; and, although the condition may arise from the toxins of bacilli in a distant part, we do not consider the disease in this section.

Treatment.—Whatever surgical means we use, or whatever plans are employed locally, it is of the first importance in lupus to place the patient under all the antituberculous conditions that have been insisted upon as necessary in other forms of tuberculosis. Fresh air, proper feeding, and sunshine are imperatively demanded; and I have always believed that the action of the direct rays of the sun upon lupoid surfaces is very beneficial.

It was in lupus particularly that positive claims were some time since put forth as to the direct value of tuberculin. Cures, or apparent cures, and cases of great improvement were reported. The profession afterward became afraid of this agent and largely abandoned its use, and it is only recently that we have become able to lay down with reasonable accuracy what we may expect from it and when it may be used. I do not believe that it cures cases of lupus; although it often produces some benefit, and sometimes extraordinary improvement. It seems to place the diseased part in a condition that favors the curative action of other remedies; and remedies that previously have proved inefficient will occasionally become efficient after the patient has received a number of doses of tuberculin.

This material is not used in every case, but only in exceptional instances. It is used when other methods of treatment have failed, and also when a patient suddenly grows worse. If given in moderate doses it is entirely safe, and moderate doses should not be exceeded. The new tuberculin of Koch is probably the best form in which to give it.

The initial dose [49] should be about 0.002 milligram; and the drug may be given every other day, the dose being increased gradually and with the greatest care. The usual amount of increase at one time is 0.002 milligram. In advancing the dose a febrile reaction greater than one degree should never be obtained. By gradual stages the dose is increased to five, six, or perhaps ten milligrams; but such a considerable dose should not be given more frequently than once a week. Tuberculin may be given in this manner for months. It seems to have been proved that, when so given, it not only favors healing and is synergistic to certain local remedies, but also renders the scar resulting from the healing less thick and deforming than if tuberculin had not been used. After a time the patient seems to develop a tolerance for tuberculin, and it then ceases to do good.

Some practitioners have recommended the hypodermatic injection of thiosinamin; but its value, to say the least, is doubtful. Others have employed calomel in emulsion given hypodermatically; but the notable benefit that has occasionally been reported when this drug has been employed may perhaps be due to the condition having been syphilitic, and not tuberculous.

A remedy that is sometimes of great value is the x-ray. In treating these cases the vacuum tube is not brought very near during the early seances. Kürnmell[50] commences with the tube at a distance of forty centimeters, and in subsequent sittings gradually reduces the distance to twenty centimeters. He never employs it for over half an hour at a time, and prefers to apply it for a quarter of an hour twice a day. The treatment may be applied for a considerable length of time; *i. e.*, a number of months. Care should be taken not to burn the patient; because, if an area of lupus is burned, the ulcer will be particularly slow in healing. The treatment should be persisted in until the lupoid ulcer has entirely healed, and most of the tuberculous nodules have passed away. The scar that results is white and does not tend particularly to contract. The question whether these healed areas are especially liable to break down again is now in the course of solution. During the time of treatment with the x-rays some drug may be used locally, either as a salve or as a lotion.

We have already said that the direct rays of the sun are beneficial in areas of lupus, and have previously stated that the elements in sunlight that benefit tuberculosis are the chemical rays, rather than the heat or the light rays. Finsen has utilized the chemical rays and applied them directly to the tuberculous area, and the results from this method have been very favorable in lupus. The Finsen light seems, beyond doubt, to have cured a number of cases; but that it has any particular superiority over the x-ray treatment has not, as yet, been conclusively demonstrated.

A remedy that was used years ago by Volkmann, and the value of which I have been able to verify by personal experience, is the local application of blue ointment. This should be diluted to the strength of about 25 per cent., should be spread upon lint, and should be applied to the non-ulcerated portion of the patch. The ulcerated portion may be dressed with gauze soaked in corrosive-sublimate solution of a strength of 1:500. That this method does tend to prevent the spread of lupus in many cases I am convinced; and not unusually, if proper constitutional treatment is employed, the area will get well.

An ointment that is used by many consists of one part of salicylic acid to eight of vaselin. Guaiacol has its advocates, equal parts of guaiacol and sterile olive oil being used. Some material is soaked in this mixture and laid upon the ulcer and the nodular margins, and the part is then covered with oiled silk.

Some form of arsenical paste is occasionally employed. The strength may be mild, so that the material is rather strongly stimulating than destructive; or it may be strong, when it acts merely as the cauterant paste occasionally employed in cancer.

A treatment that is sometimes valuable is the application of lactic acid (full strength) for half an hour twice a day, a piece of absorbent cotton being soaked in the acid and laid upon the part. When the lactic acid is removed, the part is dressed with boric-acid ointment.

In most cases the area of lupus should be treated by a surgical operation. If the location admits of it, and if the destruction has not been too great, the lupoid area should be extirpated with a knife, and the raw surface be once covered with Thiersch skin-grafts. If this is not done, the next most efficient method is to curette the area of lupus thoroughly with a sharp-edged spoon, arrest the hemorrhage by pressure, cauterize the new surface with caustic potash or pure carbolic acid, dress the part antiseptically until granulations begin to form, and then use boric-acid ointment. In performing either of the above-mentioned surgical operations, the patient should be anesthetized with nitrous-oxid gas or with ether.

Another mode of treatment, known as scarification, has some warm advocates. Nitrous-oxid gas is given the patient; a number of incisions are made in the part, the incisions being parallel and about a quarter of an inch apart, and going completely through the diseased area; then incisions are made across this area in the same manner; and the hemorrhage is arrested with pressure, and the part dressed antiseptically.

TUBERCULOSIS OF OTHER TISSUES AND ORGANS.

Tuberculosis of the Blood-vessels.—We have known for some time that the walls of veins may become tuberculous. This seems to have been pointed out by Weigert and Hannau. Koch pointed out that small arteries are occasionally attacked by the process. It is very uncommon to find large arteries tuberculous, but occasionally they are so. Dr. George Blumer, of Albany, reported, a few years ago, a case of tuberculosis of the aorta; and other cases are on record.

Vascular tuberculosis may be caused by the implantation of infective material from the blood-stream or by the direct extension of a perivascular tuberculous process. Many cases of tuberculous kidney seem to have originated in and about the arteries, and the same is true of tuberculous meningitis and of tuberculosis of other regions. The disease causes thickening of the vessel-wall, and thrombosis may occur; or in an area of softening of the vessel-wall perforation occurs and hemorrhage ensues. If an area of tuberculosis becomes adherent to a vein, and if the vein-wall softens and the tuberculous products suddenly break into the vein, hordes of bacilli are distributed to distant parts of the body and general tuberculosis arises.

Tuberculosis of the Heart.—Tuberculosis of the myocardium sometimes occurs. It is always a secondary process. The bacilli usually reach the heart-wall by way of the lymphatics, but sometimes by way of the blood-vessels. Tuberculosis of the myocardium is very seldom encountered, except, perhaps, in acute miliary tuberculosis and occasionally in tuberculosis of the mediastinal glands. The condition may be secondary to tuberculosis of the pericardium.

Certain functional disturbances of the heart that are not due to direct tuberculous disease of its wall, its covering, or its lining, are occasionally encountered in tuberculosis of distant points. The toxemia may be responsible for various cardiac aberrations. Tachycardia is by no means uncommon in tuberculous toxemia. It should also be borne in mind that tachycardia may arise from the pressure of tuberculous glands of the neck upon the nerves going to the heart.

Tuberculosis of the Brain and its Membranes.—The dura mater is occasionally, although not very often, attacked by tuberculosis—tuberculous pachymeningitis. This condition of the dura may be secondary to tuberculosis of the bones of the skull or to tuberculosis of the brain and the piarachnoid; and in very unusual cases the bacilli reach the dura from a distance by way of the blood. Sometimes the bacilli come from tuberculous lesions of the pharynx, the nasal fossa, the orbit, or the middle ear, gaining access along lymph-paths. It is the outer layer of the dura that first suffers in bone tuberculosis, and the inner layer may become secondarily involved. In tuberculosis of the piarachnoid the inner layer of the dura may become diseased first, the outer layer becoming involved later or not at all. If tuberculosis of the dura arises because tubercle bacilli have been brought from a distance by the blood, it is the inner layer that suffers first, as a rule. In tuberculous pachymeningitis there may be small tubercles or large tuberculous masses, which, perhaps, are mistaken in some cases for sarcoma. The pia and arachnoid are far more apt to suffer from tuberculosis than is the dura. Tuberculous inflammation of the pia and arachnoid is called tuberculous leptomeningitis. In the vast majority of cases the disease begins about the vessels of the pia, the bacilli having been brought by the blood.

The process may start at one or more points; and may remain localized for a considerable length of time, or may become widely diffused. Sometimes it is disseminated throughout practically the entire area of the membranes. The convexity may be affected alone or with the base. Basal tuberculosis is vastly more common than is tuberculosis of the convexity, and the process may remain limited to the base or may diffuse itself.

Although tuberculosis of the pia and arachnoid is most often of hematogenous origin, cases occasionally occur secondarily to tuberculosis of the dura of the brain. It is probably seldom that tuberculous meningitis of the piarachnoid is a primary condition; for even when the bacilli are brought by the blood, they come from some area of tuberculosis—particularly the lungs. The disease begins with the formation of miliary tubercles. In some cases a large mass, two masses, or several masses of tuberculous granulations form. A solitary mass of tuberculous material is regarded clinically as a brain-tumor.

Tuberculous meningitis is much more common in children than in adults, but it does occur even in the latter. It may be very acute in progress, the patient perishing in a few days; or it may be chronic, lasting weeks and even months, and perhaps resulting in recovery. Two distinct forms, the acute and the chronic, are found in children; but in adults it is not possible to classify so positively the manifestations of the disease.

When tuberculous meningitis arises about the vessels of the pia, the cerebral structure underneath is quickly involved, and the condition is then known as tuberculous meningo-encephalitis. In some of the cases of tuberculous lepto-meningitis there is an extensive serous effusion into the subarachnoid space; and in others there is an extensive serous effusion within the ventricles, or in both the ventricles and the subarachnoid space. The disease may spread along the choroid plexus and the velum interpositum, and enter the lateral ventricles, thus producing the effusion; or the effusion may result from the tuberculous inflammation blocking the communication between the ventricles and the subarachnoid space. In some unusual cases tuberculosis seems to begin in the lining of the ventricles. The solitary tubercles that occasionally form in the meninges or the cortex of the brain, which have already been referred to, may reach a considerable size, sometimes even as large as an English walnut or an egg. Any tuberculous area in the brain or the membranes may pass through any phase of change that a tuberculous focus elsewhere may pass through.

Whereas tuberculosis of the membranes or of the brain usually terminates fatally, a cure occasionally takes place by encapsulation in fibrous tissue or calcification of the tuberculous mass. A solitary tuberculoma may exist for a long time without giving rise to dissemination of the bacilli through the lymphatics; yet, sooner or later, this occurs in the vast majority of instances.

It is noticeable that most of the patients that develop tuberculous meningitis have been weak and sickly for some time before the beginning of the attack, this being due to an antecedent tuberculous lesion, which may be osseous, articular, visceral, or glandular; but which is usually pulmonary. Some few subjects, however,—and most of them adults,—appear to be robust and strong when the attack starts; and if any other tuberculous lesion exists, its presence cannot be determined, and it is not active. In any chronic case of tuberculous meningitis there may be distinct remissions, which perhaps deceive one into believing that a cure has been effected.

The area of tuberculosis may become the seat of a secondary infection with pus-producing organisms, and then a seropurulent fluid quickly forms. In tuberculous conditions of the brain or its membranes lumbar puncture may give the surgeon important information. He may find the cerebrospinal fluid turbid, perhaps containing pus, and not unusually containing the bacilli of tuberculosis. The exudation in basal tuberculous meningitis compresses nerve-trunks and gives rise to irritation and then to paralysis in the area supplied by the compressed nerves. It is not at all unusual for the ophthalmoscope to disclose tubercles in the choroid. Tuberculous meningitis or meningo-encaphalitis may develop in the course of acute miliary tuberculosis; although, if it does, it is seldom identified, the symptoms being merged into those of the general malady.

Tuberculosis of the Spinal Cord and its Membranes.—This is not nearly so common as tuberculosis of the brain or its membranes. It usually begins as tuberculous inflammation of the membranes, the cord suffering secondarily. There is, however, such a thing as primary tuberculosis of the cord, tumor-like masses forming, undergoing caseation, and causing pressure-signs and degeneration of the nerve-trunks. There also may be miliary tubercles widely disseminated, the bacilli having been obtained from the blood. Sometimes tuberculosis of the cord or its membranes is associated with tuberculosis of the brain or its membranes, the former trouble being then usually secondary to the latter; although occasionally the brain-disease is secondary to the cord-disease.

Tuberculosis of the dura is usually secondary to tuberculous disease of the vertebræ; and it may remain limited to the dura, constituting tuberculous pachymeningitis, or may pass to the pia and the arachnoid, constituting tuberculous leptomeningitis. If the pachymeningitis is secondary to vertebral disease, the tubercles are at first external, and the inner surface of the dura may suffer secondarily. Tuberculosis of the pi-arachnoid may be of hematogenous origin, the disease beginning about vessels of the pia. In tuberculosis of the cord and its membranes the nerve-roots are compressed by the exudation, and zones of paralysis result from pressure on the nerve-roots and on the tracts of the cord.

Tuberculosis of the cauda equina occasionally develops.[51]

Tuberculosis of the Nerves. — It is well known that the pressure of a tuberculous gland may cause neuritis; but this may be due to pressure alone, and not to bacilli. The nerves resist infection so strongly that they have been called the aristocrats of the tissues, often remaining uncontaminated when the surrounding structures are going down in ruin. Just as the pressure of a tuberculous gland on a nerve may cause pressure-neuritis, so the pressure of a tuberculous mass at the base of the brain or in the spinal canal may cause pressure-neuritis. There is probably, however, such a thing as a true tuberculous neuritis, the bacilli attacking the nerve-sheath or the nerve itself, symptoms resulting that are not due purely to pressure. Occasionally, when a tuberculous lesion exists somewhere in the body, particularly if it exists in the lungs, multiple neuritis develops; and we call this tuberculous multiple neuritis. Bacilli are not found in the nerves; and the inference is that the bacilli of tuberculosis form a poison, and that this poison attacks the nerves. In making the diagnosis of tuberculous multiple neuritis it is necessary to exclude alcohol as a possible cause.

Tuberculosis of the Mammary Gland.— This is a rare condition, but is more common than used to be supposed. In times past it is probable that the diagnosis has frequently been missed. The condition has, however, been recognized for many years, and seems to have been first pointed out by Sir Astley Cooper. It is infinitely more common in the female than in the male.

In mammary tuberculosis the bacilli may enter through an abrasion of the breast or nipple, may be driven in by friction of the nipple or skin, and may ascend the milk-ducts or the lymph-vessels of the nipple. Secondary tuberculosis of the mammary gland may follow tuberculosis of the axillary or subclavian glands, caries of the ribs or sternum, or tuberculous empyema. In some cases the bacilli are brought by the blood from a distance; for instance, from an area of bone-disease in the extremities or from a focus of pulmonary tuberculosis. Most of the patients are between thirty and forty years of age. There is some evidence that chronic mastitis predisposes to the disease. Scudder says that half the reported cases have been in persons that have borne children.

The condition is slow in onset, very chronic in progress, sometimes painful, and sometimes painless. The breast may be enlarged, but is usually small and nodular; sometimes it is actually shrunken. The diseased breast may be filled with small indurations, may contain large nodules, or may hold great softening masses covered with discolored skin. Tuberculous abscesses may form and discharging sinuses arise. The axillary glands are practically always diseased, and the best treatment is to remove the mammary gland and clear out the axilla.

Pulmonary Tuberculosis from the Surgical Standpoint.* — As long ago as the seventeenth century, Baglivi attempted to tap and inject tuberculous cavities in the lung; and from that period down to the present, daring experimenters have now and then tried it again. A number of years ago Mosler introduced a trocar into a tuberculous cavity and injected into the cavity a solution of permanganate of potassium, and in 1874 Dr. Pepper attempted to revive the method. Injections of a solution of corrosive sublimate thrown into the pulmonary parenchyma about a tuberculous focus were employed by Hillier. The above-mentioned attempts were without therapeutic value, and were merely hazardous experiments.

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*For a full consideration, see section on Surgery of the Respiratory Organs.

During recent years efforts have been made to place the surgical treatment of pulmonary tuberculosis on a scientific footing. Although many operations have been performed and some cures have been reported, the question is still unsettled; and the opinion remains general among surgeons that the field of operative surgery in pulmonary tuberculosis is narrow and strictly limited. The operations for this condition may be classified as follows:

1. The aspiration and injection of tuberculous cavities.
2. The incision and drainage of tuberculous cavities.
3. The incision and drainage of tuberculous abscesses.
4. The excision of tuberculous areas.
5. The collapse of the lung by rib-resection or by the creation of artificial pneumothorax.

The aspiration and injection of tuberculous cavities is an utter failure, and need not even be considered. Incision and drainage of tuberculous cavities is practically useless. In fact, as Verneuil has said, if there is a cavity, it is seldom proper to operate at all. The localization of a cavity is more or less uncertain, even with the aid of the x-rays, and cavities are frequently multiple. It is only when the patient is in good general condition and there is a single large cavity that good may be hoped for from drainage, but these are among the very cases that occasionally, though of course seldom, recover without any operation.

Incision and drainage of tuberculous abscesses of the lung has nearly always been a failure, although some favorable results are upon record. The operation employed for this purpose is known as *pneumotomy*. It is to be considered only in a unilateral tuberculous abscess, or when a surgeon operating for pus in the pleural sac finds the evidences of an adjacent tuberculous pulmonary abscess. The incision of the lung should be made with the Paquelin cautery. The operation is out of the question if there are multiple or bilateral abscesses. In a solitary abscess, when the cavity is not definitely circumscribed, operation is not advisable. In any rapidly-progressing case, or in any case in which the disease has become stationary, it is extremely injudicious to intervene; as these are the cases that may recover without operation. These operations have a very high mortality-rate; and even when the patient recovers from the operation, although the local condition may be improved, it is not cured. In fact, it is extremely rarely that pneumotomy is justifiable in tuberculous abscess of the lung. It is certainly justifiable only when mixed infection has taken place. In such a condition operation may be demanded.

Excision of a tuberculous focus is known as *pneumectomy*. Recoveries from this operation have been reported, and some few surgeons have advocated it; but the general opinion of the profession is that it is not to be performed.

Nature endeavors to cure tuberculosis of the lung by the formation of fibrous tissue, and this tissue contracts; but the rigidity of the chest-wall prevents great contraction, and hence hinders the tendency to cure. In 1891 Dr. Oscar H. Allis advocated rib resection as a possible means of curing pulmonary tuberculosis. Some operations of this sort have been performed with apparent advantage. The cases to which the procedure is adapted are those in which the disease is one-sided and very extensive, and in which there is a definite tendency to retraction of the chest-wall. Porritt has advocated rib resection in apical phthisis, removing ribs front and back. This operation, however, carries with it decided elements of peril; and its actual curative power is uncertain and limited.

It has long been known that the development of serous pleurisy or of pneumothorax during the existence of pulmonary tuberculosis may apparently prove of distinct benefit. In serous pleurisy the lung is compressed and is, so to speak, put at rest; in pneumothorax it is decidedly compressed and absolutely put out of function. The benefit of rest is thus secured to the diseased part, the curative fibrous tissue has an opportunity to form, and contraction is favored. Some surgeons have endeavored deliberately to induce serous pleurisy; but when this is done, empyema is very likely to arise.

Farlanini and Murphy have advocated, in certain cases, the establishing of artificial pneumothorax and Murphy has used nitrogen-gas for this purpose. The value of the method is still not positively determined, although it seems quite clear that it is reasonably free from danger; that it will certainly arrest pulmonary hemorrhage; and that in some cases it can, at least, retard the development of the tuberculous process. There are, however, many problems in relation to the application of this method and the cases to which it is suited that still remain unsolved.

Tuberculous Pneumothorax.—This condition is due to the softening of a tuberculous pulmonary area and perforation of the visceral layer of the pleura. Beyond any doubt, an enormous majority of all cases of pneumothorax are of tuberculous origin. This symptom, as pointed out by John Lovett Morse, is usually of gradual onset, but occasionally comes on suddenly; and the characteristic combination of symptoms is violent pain with dyspnea. We have already referred to the fact that when pneumothorax develops the tuberculous condition in the lung may be arrested or apparently cured. It is advisable, perhaps, to operate on certain of these cases; although some physicians have been inveterately opposed to operation. For a number of years I have pursued the plan advocated by West, which is as follows:

In a recent case, do not operate unless the symptoms become intensified. If it becomes necessary to intervene, puncture with a trocar, employing no suction whatever; and repeat several times, if necessary. If tapping brings relief of the urgent symptoms, do nothing more radical; but if it fails to bring relief, make an incision in an intercostal space. If pyopneumothorax arise, as it is very liable to do, a portion of a rib or ribs must be resected to permit drainage.

Tuberculosis of the Pleura.—Tuberculosis of the pleura may be primary, but is usually secondary to tuberculosis of the lungs or of the mediastinal glands, or forms a part of a general tuberculosis. Primary pleurisy not due to trauma is usually, if not always, tuberculous in origin. In some cases of tuberculosis of the pleura the membrane is covered with miliary tubercles; in some, tubercles are gathered here and there into definite areas; and in some, the pleura becomes enormously thickened. Over a tuberculous focus in the lung there is usually a thickened area in the visceral layer of the pleura. Such areas are the great cause of chest-pains in tuberculosis, and such an inflamed and thickened area of the pleura may or may not become tuberculous. The effusion into the pleural sac in tuberculosis of the pleura may be serous or may consist of tuberculous pus. If mixed infection occurs, it will become true pus. The effusion in the purely tuberculous process rarely contains living bacteria; although they, of course, exist in numbers in the granulation tissue of the diseased pleura. A tap that exhibits sterile fluid is an indication but not a proof of the tuberculous nature of the process. If the fluid contains pus-germs, it does not, however, prove the non-tuberculous nature of the process; because one may be dealing with a tuberculous process that has undergone secondary pyogenic infection.

In tuberculous pleurisy it is not advisable to aspirate early but aspiration should be performed if the effusion displaces the heart considerably and distinctly increases the dyspnea. If secondary infection occurs and the effusion becomes purulent, a portion of a rib should be resected and a drainage-tube inserted.

Tuberculosis of the Pericardium.—This condition may be primary, but it is usually secondary to pleural tuberculosis. Autopsies upon patients dead of phthisis show that about one out of every hundred exhibits tuberculous pericarditis. There is a miliary form of pericardial tuberculosis, and a form in which both pericardial layers are enormously thickened and in which caseous degeneration takes place. It is in the latter cases that extensive pericardial adhesions form.

Tuberculosis of the Peritoneum.—This condition is considered at length in another section of this work. It is sufficient here to call attention to a few fundamental facts:

It is occasionally, although seldom, primary. In a great majority of the cases distant foci of tuberculosis exist, and in at least half the cases the lungs are involved. In a great many cases supposed to be instances of primary tuberculosis of the peritoneum there is really another focus of disease that is not demonstrable. Tuberculous peritonitis may form a part of a generalized tuberculosis, it may follow a tuberculous intestinal lesion, tuberculosis of the appendix, or tuberculosis of the mesenteric glands; or the bacteria may enter by way of the Fallopian tube, the blood, or the lymph. When the primary lesion is disease of the abdominal lymph glands, the cecum is liable to be attacked. Women suffer more frequently from the disease than men, and the period of greatest liability is between the ages of twenty and forty years.

The cases are divided into two groups: the chronic form, which is by far the most common; and the acute condition, which resembles, in many cases, acute appendicitis. In tuberculous peritonitis it is common to find an associated cirrhosis of the liver. Chronic tuberculous peritonitis may present itself in the ascitic, the fibrinoplastic, or the caseous form; although these forms are only stages of the same disease. The disease may exist for a considerable length of time without giving rise to any symptoms, and in this condition acute symptoms may suddenly develop or intestinal obstruction may suddenly take place. In most cases, however, the symptoms appear insidiously and gradually and progressively grow worse.

Tuberculosis of the Alimentary Canal.—*Tuberculosis of the stomach*[52] is extremely rare, the gastric juice being hostile to the tubercle bacilli. There is a hypertrophic form and an ulcerative form. I operated in the Jefferson College Hospital on a girl of sixteen years for perforated ulcer of the stomach in which the condition was tuberculous and was associated with a tuberculous abscess in front of the stomach and enlargement of the abdominal glands. The abscess had undergone secondary infection.

Intestinal tuberculosis may result from tuberculous peritonitis or from tuberculous abdominal glands; but it may be a primary condition, arising in the mucous membrane of the bowel. Primary tuberculosis of the intestine is certainly very rare, the tubercle bacilli readily passing through the intestinal wall and seldom producing an intestinal lesion.[53] Intestinal tuberculosis may develop in a person with pulmonary tuberculosis or some other distant tuberculous lesion.

Intestinal tuberculosis may cause obstruction, abscess, or perforation. A genuine tuberculous appendicitis occasionally occurs,[54] and I have seen a huge tuberculous abscess associated with this condition. Tuberculosis of the cecum [55] is sometimes encountered, particularly of the form in which there is an enormous production of granulation tissue—the form that simulates tumor-formation and is known as hypertrophic tuberculosis of the cecum. Ileocecal tuberculosis was discussed at the Congrès Internat. de la Tuberculose, held at Paris in 1905. Demoulin points out the existence of an ulcerating form, a hypertrophic form, and an entero-peritoneal form. The appearance of an area involved by the latter form is exactly similar to some conditions produced by appendicitis. Tuberculosis of the appendix does occur, but is very rare.[56] As Bérard says, the appendix is usually involved in cecal tuberculosis; but it may be involved when the cecum is free. Tuberculous appendicitis may be secondary to tuberculous peritonitis (Mayer). Sometimes an appendix in a hernia becomes tuberculous secondarily to tuberculosis of the hernial sac (Cornil), or to tuberculosis of the female genital organs, the infection having passed along the appendiculo-ovarian ligament. An anal fistula is frequently tuberculous in origin; and when it is tuberculous, the lungs have usually been antecedently affected.

Tuberculosis of the Liver.[57]—This condition is practically always secondary to some other tuberculous process, and can rarely be diagnosticated during life. It is most commonly encountered in tuberculosis of the peritoneum or of the intestine, but it may form a part of a generalized tuberculosis. It is possible that in very rare instances primary tuberculosis of the liver occurs. There may be tuberculosis of the bile-ducts; a caseous mass or masses may form in the liver; or a tuberculous abscess may form. Tuberculosis of the liver may cause cirrhosis.

Tuberculosis of the Pancreas.—This is an extremely rare condition, although a few instances of it have been reported. Some years ago the statement was made that the pancreas does not participate in general tuberculosis; but this statement has been proved to be incorrect. Sometimes an isolated tuberculous mass of considerable size forms, the condition having probably begun in the lymph glands that are contained in the substance of the pancreas. Such a tuberculous area may burst into the stomach, an instance of this having been reported. Sendler successfully removed a tuberculous mass from the head of the pancreas.

Tuberculosis of the Spleen.—Tuberculosis of the spleen is seldom met with, although it is occasionally found during the existence of a chronic abdominal or chronic pulmonary tuberculosis. The spleen may also be involved in acute miliary tuberculosis. A form that is occasionally met with in tuberculous children, and even in older persons, causes the spleen to look, on a cursory examination, as if it were involved in a malignant tumor. The organ is decidedly enlarged and, when sectioned, is found to have nodules on the surface and within it,—many of these nodules being, perhaps, as large as an English walnut.

Tuberculosis of Muscle.—This is seldom encountered. It is almost never primary, although there are some reported cases. Secondary muscular tuberculosis is seen in association with bone disease and chronic abscesses adjacent to the muscle.

Tuberculosis of Fascia.—This form of tuberculosis has been described particularly by the elder Senn,[58] by J. E. Moore,[59] and by J. Clark Stewart.[60] It is by no means uncommon. It may be primary, the bacilli arriving through the blood or lymph, and no other focus of tuberculosis existing; or it may be secondary, the bacilli coming by way of the blood or lymph from a near or distant focus, or the near focus gradually coming into immediate contact with the fascia. Secondary fascial tuberculosis is seen particularly in the neck, from softened lymph glands; in the back, from vertebral caries; and in the thigh, from a tuberculous joint or bone. The disease may assume the form of a tuberculous abscess, the walls of which are densely fibrous and are lined with tuberculous granulations.

In the primary form there is great thickening of the fascia. The process begins at one or several points and gradually spreads. The foci caseate and sinuses form. This spreading form of fascial tuberculosis is extremely dangerous; and cure can usually be effected only by free extirpation of the diseased fascia, as is recommended by Stewart.

Tuberculosis of Tendon-sheaths.—This condition may be primary or secondary, the latter form being much the more common, although the primary form is met with not unusually. The secondary form is encountered in association with a tuberculous joint. In one form of tuberculosis of a tendon-sheath there is the formation of a fungus-like mass of granulation tissue. Such a mass sometimes entirely wraps the tendon around, and occasionally caseates. In the other form of the condition, small tuberculous granulations form on the inner surface of the sheath. These undergo fibroid changes, are loosened, and freely move about the sheath and the tendon. They are called *rice-bodies* or *melon-seed* bodies, and when they exist there is usually a considerable amount of serous effusion in the tendon-sheath. The condition with considerable effusion is frequently spoken of as *hygroma*, and sometimes as *compound ganglion*. These conditions are considered fully in the special sections of this work.

Tuberculosis of Bursæ.—Just as in tendon-sheaths, so a bursa may become the seat of fungus-tuberculosis, of serous tuberculosis with the formation of melon-seed bodies, and of caseation.

Tuberculosis of Bones.—The condition is very common, particularly in the young, and is frequently preceded by a sprain or contusion, which constitutes a point of least resistance. The bacteria that reach this point of least resistance may come directly from the blood or lymph or may arrive, as inhabitants of an embolus, from a tuberculous focus far away—perhaps in the lung, a lymph gland, or some other structure. When such an embolus reaches the end of a long bone, it is arrested in a terminal artery; and a wedge-shaped infarct results. Tuberculous bone disease of a long bone begins, as a rule, just underneath the articular cartilage or in the epiphysis of the bone. The products of the inflammation may be absorbed, may undergo fibrous encapsulation, or may caseate.

Tuberculosis of Joints.—An old name for tuberculosis of joints is pulpy degeneration of the synovial membrane. Tuberculous joint disease is far more common in youth than in old age, although two joints particularly—that is, the wrist and the shoulder—are rather prone to suffer in adult life. Joint-tuberculosis, like tuberculosis of the bones, is frequently preceded by a slight injury. As a rule, the disease begins in the head of the bone; dry caries takes place, and necrosis follows; or perhaps a tuberculous abscess forms, which breaks into a joint. Occasionally the disease begins as a synovial tuberculosis. This not unusually occurs in the knee-joint.

Glandular Tuberculosis.—Tuberculosis of the lymph glands has been previously spoken of as the most characteristic manifestation of the so-called scrofulous state, and is due to the arrest of bacteria from the lymph-stream. It is known as tuberculous adenitis. This form of tuberculous infection is in many instances extremely mild. It tends rather to remain localized than to generalize; and if it does remain local, complete recovery follows. If the gland is healthy, it stands as a sentry on the banks of the lymph-stream; captures the bacteria as they arrive, and holds them prisoners until they are destroyed. In this process the gland, owing to physiologic necessity, enlarges in the endeavor to destroy the micro-örganisms. It may hold and destroy all the bacilli, or some few may get into adjacent glands and there be destroyed. If the tissue-resistance is less active, or if the bacilli are more numerous or more virulent, periglandular inflammation occurs and a protective inflammatory barrier surrounds the gland, for the purpose of encompassing the area of infection. In a great many instances the glands caseate; and the caseated material may slowly reach the surface, or an adjacent cavity or viscus, and finally escape. When caseation takes place, the area is usually surrounded by encompassing fibrous tissue. The caseated area, as previously described, may become a cold abscess or the seat of secondary pyogenic infection. If the glands fail in their protective labor, then the bacilli are widely disseminated throughout the organism, and tuberculosis arises in various structures. If a softened tuberculous swelling should happen to break into a blood-vessel, the disease is certain to be disseminated.

Tuberculous adenitis is most frequent between the third and the fifteenth years. In tuberculosis of the glands of the neck the condition is not unusually preceded by slight enlargement resulting from catarrhal inflammation of the mucous membrane of the mouth. Sometimes a tuberculous gland is cured by fibrous encapsulation, fibrous transformation, or calcification; but long after the tuberculous gland has apparently healed, it may break down again and soften, forming a residual abscess. Actual suppuration, due to mixed infection, may occur. Tuberculous glandular enlargement is usually restricted to a limited area, although occasionally it may be widespread. A person not recognized as of the tuberculous type may develop this condition, but the most common victims are those of the tuberculous type. It is probable that bacilli are constantly entering the lymph-glands and are constantly being destroyed, having been taken up from wounds or surfaces which the lymphatics drain. Again, the bacilli may enter the glands and remain there, not being immediately killed, but remaining latent,—sleeping, as it were,—perhaps for a considerable period of time; and afterward awakening to activity and waging destruction. The chief areas of glandular tuberculosis are the regions of the cervical, mediastinal, mesenteric, and retroperitoneal glands. It is by no means rare, however, to find tuberculosis of the iliac, inguinal, or femoral glands; and I have seen tuberculosis of the supratrochlear and also of the popliteal glands. There is considerable evidence that certain cases at least of supposed Hodgkin's disease are due to the action of the bacilli of tuberculosis.

Tuberculosis of the Kidney.—Genuine primary tuberculosis of the kidney begins in one kidney; and no other tuberculous area can be demonstrated in the body, the bacteria having been obtained from the blood. Usually, although the lesion is first one-sided, there is some distant focus of tuberculosis; perhaps there always is, although it cannot always be recognized. This unilateral condition is very apt soon to become bilateral, the disease having passed from one kidney to the bladder, and having afterward affected the other kidney by ascending secondary infection. These conditions of so-called primary tuberculosis of the kidney are rare; and the disease is far more common as a process secondary to tuberculosis of the prostate, bladder, or epididymis. In such secondary cases both kidneys are involved practically at the same time. Tuberculosis of the kidney is more common in males than in females, and is particularly common between the twentieth and the fortieth year of life.

Tuberculosis of the Adrenals.—This is the most common disease that is found in the adrenals. It seems reasonably probable that what is known as Addison's disease is due to tuberculosis of these structures, although it has also been shown that tuberculous areas may be found in the adrenals without the symptoms of Addison's disease.

Perirenal Tuberculous Abscess.—This condition may be associated with tuberculosis of the kidney or with vertebral tuberculosis, but it may occur as an independent condition. It begins as a chronic inflammation of the retrorenal cellular tissue. It may terminate in fibrous-tissue formation, in caseation and cold abscess, or in mixed infection. In the latter condition an ordinary perirenal abscess forms.

Genito=urinary Tuberculosis.—We have referred briefly to tuberculosis of the kidney. Tuberculosis of other parts of the genito-urinary system is discussed at length in the sections of the book devoted to genito-urinary surgery.

Tuberculosis of the Middle Ear.—This condition may merely involve an inflammation of the mucous membrane of the middle ear, but usually it is a condition of tuberculous bone disease. There may be extensive destruction of bone, and abscess-formation may result from mixed infection.

Tuberculosis of the Ischiorectal Fossa.—This is discussed in the article on ischiorectal abscess.

Tuberculous Anal Fistula.—This is discussed in the article on anal fistula

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CHAPTER XIX.

CHANCROID.

By Edward Martin, M.D.,

PHILADELPHIA.

Chancroid, sometimes called soft chancre, is a venereal ulcer, inflammatory and destructive in type, contagious, auto-inoculable, and frequently complicated by necrosis of the lymphatic glands in immediate anatomic relation with the surface involved.

It has no distinct period of incubation, is steadily and rapidly progressive, and runs its course in from four to six weeks. It may be inoculated upon any skin or exposed mucous surface, but is usually found on or about the genitalia. It is essentially a disease of the ignorant and uncleanly.

Cause.—Chancroid is probably due to a specific strepto-bacillus; described by Ducré as short and thick with rounded ends, much resembling a dumb-bell, half a micromillimeter in length. It is stained by the following solution:

5 per cent. boric solution	½ oz.
Saturated aqueous solution methyl blue	5 drams.
Distilled water	6 drams.

Cover-glass preparations are floated in this dye for half an hour, then washed in distilled water, dried and examined.

The evidence as to the specific nature of these microörganisms is not complete, since chancroids have not yet been caused by the inoculation of pure cultures grown on artificial media. None the less it has been shown by competent observers that the Ducré bacillus is always found associated with the ordinary bacteria in every chancroidal lesion, and if successive inoculations be practised under aseptic precautions the discharge from the first set of inoculation pustules being used to produce a second set, and that from the second set for a third, apparently pure cultures of the Ducré bacillus may be obtained which by inoculation will produce chancroid.

The lesion, even in vigorous persons, runs a typical course, differing distinctly from that of the ordinary infected wound.

Finally, a thorough cauterization of a rapidly extending chancroid will convert it into a simple ulcer, which quickly heals though it teems with the ordinary germs of suppuration.

The chancroidal virus requires favoring conditions for its development. Its specific property is destroyed by moderate heat and feeble germicides.

Before the pus from a chancroid can produce a similar lesion elsewhere it must be rubbed into a surface-break. This break may in the case of auto-inoculation be due to maceration and abrasion, as shown by the frequent development of chancroids upon skin surfaces rubbed by the original lesions. The etiology is the same when chancroid is contracted during sexual contact of one person with another, the points of entrance in the latter case being herpetic lesions or fissures or cracks which have been thoroughly traumatized during the sexual act.

The virulence of the chancroidal discharge decreases in proportion to the age of the lesion, the pus in the later healing stages producing at most a superficial inflammation such as would be incident to inoculation from the discharges of any simple sore.

Development of the Chancroid.—At the seat of inoculation there develops, usually within the first three days, a pustule which by the time it comes under observation has become a gray, sloughing, punched-out, ragged, and undermined ulcer with distinct, bright red, inflammatory areola. This ulceration increases in all dimensions with considerable rapidity, and in three or four days will exhibit some undermining of the edges and a marked surrounding edema. It may remain superficial throughout its entire course.

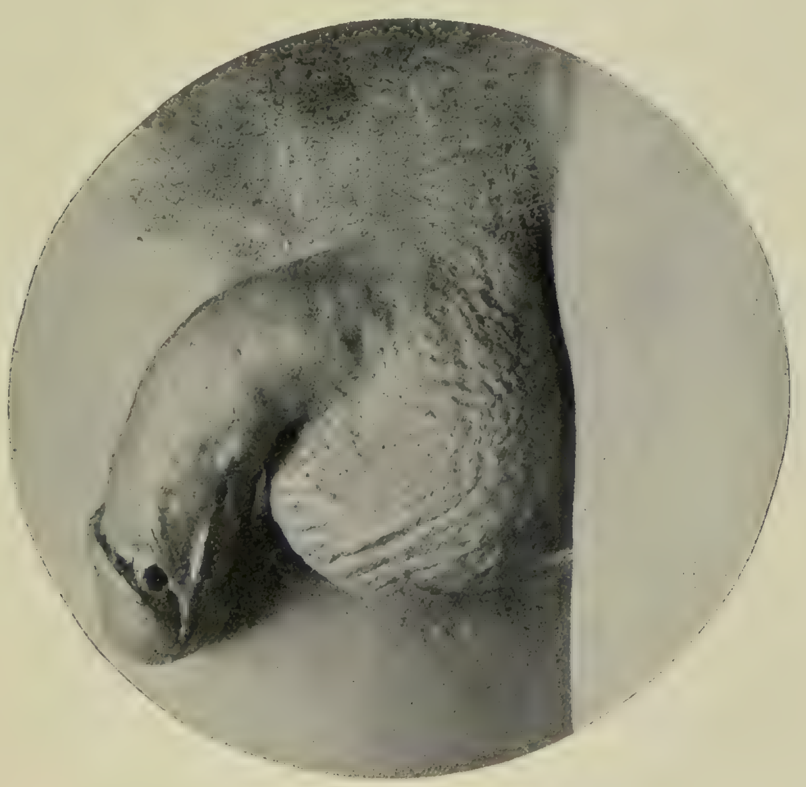


FIG. 166.—FOLLICULAR CHANCROID (White and Martin).

The follicular form begins as a furuncle with a red, hard, ulcerating center, a red areola, and pronounced inflammatory edema. In place of discharging pus and promptly healing, as is the case with a boil, it extends peripherally, forming a jagged, undermined, deep, crater-like ulcer. The extension, however, is less rapid than is customary with a superficial chancroid unless the lesion be mechanically or chemically irritated.

The shape of the chancroid in the beginning is dependent upon that of the lesion through which its specific poison gained entrance. Thus, if inoculation has taken place through a hair-cut, there will at first be a linear ulcer; if herpes have opened the way for infection, there will be multiple ulcers with the typical herpetic outlines; a follicle on becoming chancroidal first forms an indurated, inflammatory lesion much like a boil. About the frenum the ulcers are prone to become linear, entirely destroying this organ. In the coronary sulcus they extend in the direction of this furrow. Around the anus the sores are usually ragged and linear.

The lesion may be superficial or deep. The inflammation may be localized or widespread and may reach a grade of such intensity as to be accompanied by sloughing or extensive gangrene.

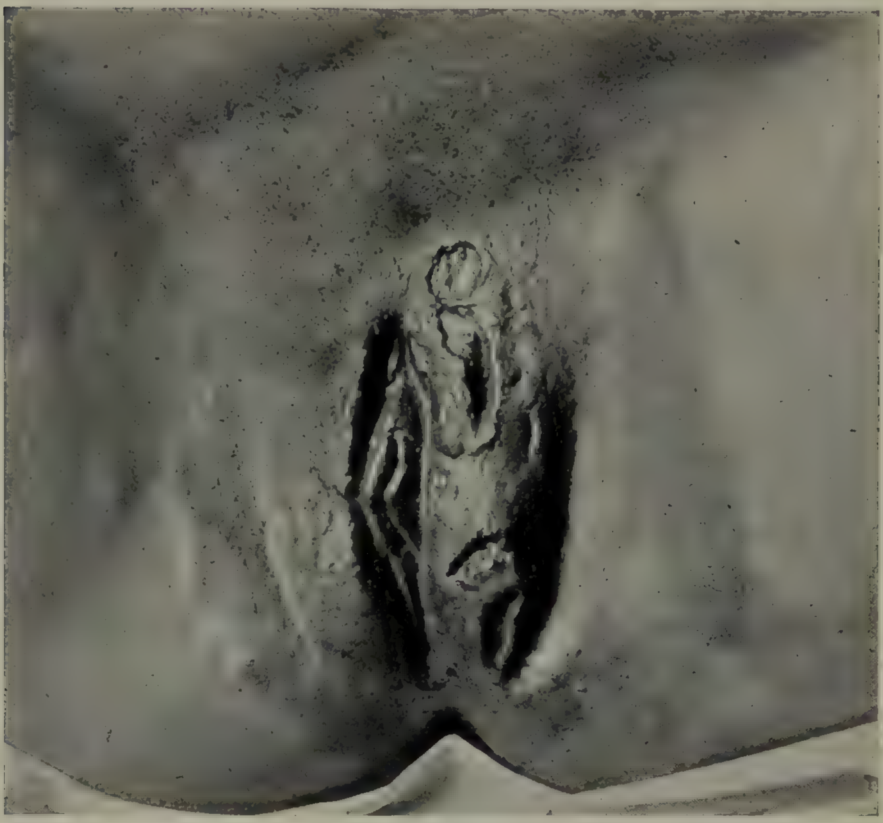


FIG. 167.—PHAGEDENIC CHANCROID (White and Martin).

The so-called serpiginous chancroid, by which is meant a huge lesion lasting for months, spreading slowly in some directions, while it heals in others, and producing extensive destruction and cicatrization, is nearly always a manifestation of late syphilis.

Seat of Chancroid.—Chancroids are usually placed behind the coronary sulcus, where they form a broken ring which in aggravated cases may by confluence be complete. They are also common on the inner surface of the foreskin, at the frenum, and about the urinary meatus and the preputial orifice. In the latter case they are usually due to auto-inoculation occurring secondarily from an infection of cracks or fissures made by the patient's efforts at retracting an edematous foreskin for the purpose of adequately treating the original lesions. They are also noted upon the outer skin of the penis and upon the scrotum and the inner surface of the thighs.

Upon the skin surfaces they commonly begin as furuncles, since they are expressions of follicular infection ultimately causing incrusted ulcers much like those of ecthyma.

Chancroids about the anus are rare in both sexes, particularly so in the male. Genital chancroids of women are noted in the fourchette, upon the inner surface of the lesser lips, about the clitoris and the inner or outer surfaces of the greater lips; exceptionally upon the vagina or the os uteri. They are also found at times on the inner surfaces of the thighs and about the anus; in the latter case usually from auto-inoculation of fissures or abrasions by a vulvar discharge trickling backward.

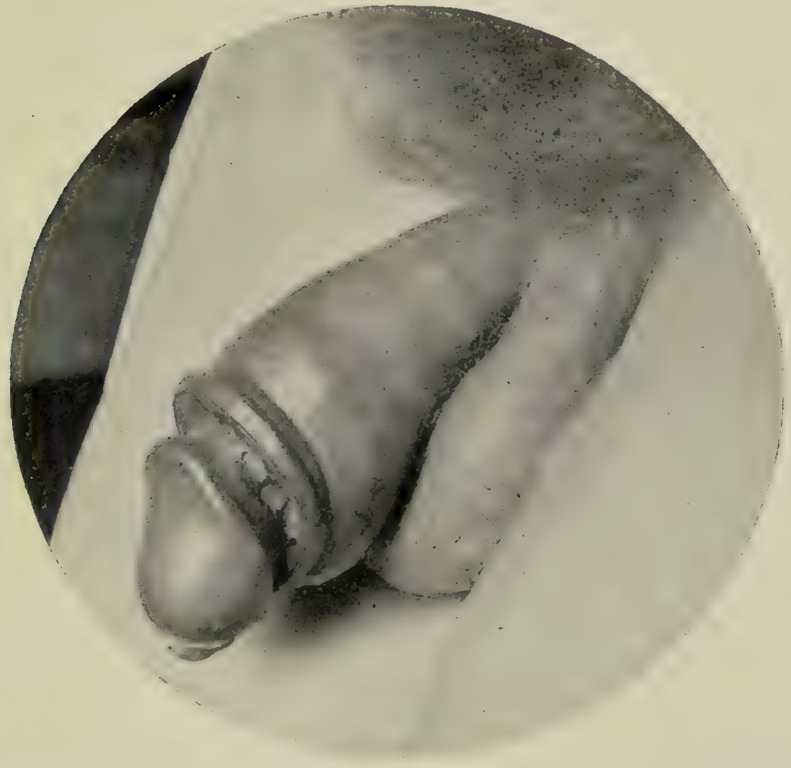


FIG. 168.—MULTIPLE CHANCROIDS OF THE CORONARY SULCUS (White and Martin).

Symptoms of Chancroid.—In its ordinary development the characteristics of chancroid are: (1) Rapid development after exposure; (2) multiplicity of lesions; (3) pustular or ulcerating from the first; (4) destructive and inflammatory in type; (5) prone to auto-inoculation, producing similar lesions on surfaces with which the discharge comes in contact; (6) absence of induration; (7) complication by inflammatory buboes.

No single one of these symptoms is sufficient in itself for the establishment of a diagnosis. Perhaps the most suggestive is auto-inoculability, that is, the development of similar sores upon surfaces with which the discharges come in contact, since this, though possible in the case of simple sores, is unusual.

There is sometimes an apparent incubation period of three to five days, due probably to a failure to detect the lesions in the early stages of their development, though it is conceivable that infectious discharge may remain without causing symptoms till a subsequent trauma prepares the way for the development of characteristic ulcers.

Though the lesion is commonly multiple, this is mainly because of the tendency to auto-infection, in which case the ulcers develop not at the same time but successively. If there have been multiple erosions or abrasions at the time of exposure to contagion, the chancroid will be multiple from the first. This is not usually the case. A single lesion treated properly from the beginning usually remains single.

Though the lesion is usually pustular or ulcerating from its incipiency, it may begin as an indurated papule, a follicle having been infected and inflaming and breaking down much as would a boil. This form of chancroid is exceptional and is likely to be confusing from the diagnostic standpoint only for the first two or three days.

Even the rule to the effect that chancroids are acutely inflammatory and destructive in type is subject to some exceptions, the sore developing slowly, remaining superficial, and giving rise to very little inconvenience through its entire course in some cases.

The tendency to auto-inoculation is particularly pronounced in chancroid and is most marked in the ignorant and uncleanly. In the coronary sulcus chancroids often entirely ring the penis. Lesions of the foreskin, if of the outer surface, are reproduced on that part of the scrotum into which the discharge is rubbed, while chancroids of the glans penis are commonly complicated by similar lesions of the apposed mucous layer of the prepuce.

Absence of induration is characteristic of chancroid except when it has been treated by cauterants or the application of such irritants as silver nitrate. Under these circumstances the lesion may exhibit an induration almost as typical and clearly marked as that which characterizes a chancre.

Inflammatory buboes are commoner complications of chancroid than of any other genital lesion, yet in well-managed cases they are the exception rather than the rule, and, moreover, they may complicate any simple infection.

Diagnosis of Chancroid.—The diagnosis will be based upon the association of symptoms. Apparently it should be made by the finding of the Ducré bacillus. This seems to be possible only to comparatively few who are thorough believers in the specific nature of this micro-organism.

The chancroid must be distinguished from simple infections, from herpes, follicular abscess, and the primary, secondary, and tertiary syphilitic lesions.

Simple infection begins much as does a chancroid, and cannot in the first few hours be distinguished from the latter. Under cleansing and protecting treatment the superficial inflammation promptly subsides, cure being accomplished in three to five days. If a simple infection is subject to repeated irritation and trauma, as from sexual intercourse, the resulting inflammation may become hyperacute and destructive in type and may closely simulate an inflamed chancroid.

Herpes remains superficial from the first.

Follicular abscess recovers promptly.

The chancre is characterized by a period of incubation rarely less than two weeks, and though in its beginning it may not be distinguishable from chancroid, its slow progression and indolent course, with the subsequent development of induration, lymphangitis, and lymphadenitis, sufficiently differentiate it from a lesion which is acutely inflammatory and rapidly progressive and is destructive of tissue from the first.

Mucous patches placed upon the genitalia may on first inspection so closely resemble chancroids as to make the differentiation extremely difficult. This is especially the case when such patches have become acutely inflamed as a result of uncleanliness or mechanical irritation. The diagnosis under such circumstances will be formulated on the history of the case and the presence of associated lesions of obviously syphilitic nature, together with the evidence afforded by the beneficial effect of appropriate constitutional treatment.

A genital gumma which has softened and discharged, because of the surrounding infiltration and its chronic course, is more commonly mistaken for a chancre than a chancroid. If, however, it becomes acutely inflamed it can be distinguished from the latter lesion only by the history of the presence of an indurated nodule which preceded by days or weeks the development of an ulcer.

Complications of Chancroid.—The complications of chancroid are phimosis, paraphimosis, gangrene, lymphangitis, and lymphadenitis.

Phimosis.—When chancroid develops beneath a long foreskin, even though the preputial orifice be sufficiently large to allow of complete retraction under ordinary circumstances, the inflammatory edema is usually so extensive as to make this retraction for cleansing purposes at first difficult and painful and later quite impossible. Incident to the resulting phimosis there is retention of discharges, added acuteness of the inflammation, and an increase of the swelling. Under these circumstances the chancroid extends rapidly and may produce extensive sloughing or even widespread gangrene. Moreover, because of lack of thorough cleanliness the development of lymphangitis and lymphadenitis is distinctly encouraged. In the case of a long foreskin which has never admitted of retraction the conditions are even worse.

Paraphimosis.—It not infrequently happens that a patient suffering from chancroid and with a long prepuce retracts the latter for the purpose of cleanliness, but because of inflammatory swelling is unable to draw it forward again. The constriction of the preputial ring causes rapid increase of edema and very shortly makes reposition without surgical operation quite impossible. The chancroid under such circumstances rapidly extends and may become gangrenous in type, or the constriction itself may be sufficient to cause extensive destruction of tissue.

Gangrene.—Extensive tissue necrosis is rarely observed in chancroid except as the result of phimosis or paraphimosis. It may, however, follow an intense exacerbation of chancroidal inflammation incident to mechanical irritation such as that caused by coitus or chemical applications sufficiently powerful to be irritating but not destructive. Under such circumstances there is usually an enormous edematous infiltration extending wide of the original lesion. The parts become cold, black, and extremely foul in odor. There are the customary constitutional symptoms of septic absorption, though exceptionally these may be absent, there being one reported case in which the patient, in walking to the hospital for the purpose of seeking medical help because of a gangrenous chancroid, found on his arrival there that the greater part of the penis had dropped off. This also illustrates the occasional great rapidity of the sloughing process, which may extensively involve the abdominal walls and may result fatally. Under such circumstances there is usually a constitutional dycrasia such as that incident to advanced Bright's disease, diabetes, cirrhosis of the liver, or parasyphilitic anemia. Exceptionally the gangrenous process is slow but persistent, forming huge serpiginous ulcers which absolutely resist all local treatment, even the actual cautery. These lesions are mostly parasyphilitic.

Lymphangitis.—This, except for a moderate thickening of the lymphatic vessels of the penis, is a comparatively rare complication of chancroid. In its complete development there will be found running along the dorsum of the penis a red, indurated cord, associated with pronounced swelling of the soft parts. At one or more points in the path of this cord the swelling may become pronounced, soften, and discharge pus. The resulting abscesses are prone to become converted into chancroids, though they are not necessarily so from the beginning.

Lymphadenitis.—Inflammation of the glands which receive the lymph from the seat of chancroid is the commonest complication of this lesion. The inflammation is acute in type and is most likely to develop in connection with lesions which are not kept clean, which are subject to mechanical or chemical irritation, or in which free drainage is prevented by the injudicious use of dusting powders. The inflamed glands or buboes commonly develop in the course of the first two weeks of a chancroid, though they may not appear for weeks after complete cicatrization of the lesion has been accomplished. They are usually multiple, but to palpation appear single because the inflammation is most pronounced in one gland and the periglandular swelling obscures the smaller tumors. They are often bilateral, especially when the chancroid involves the frenum. As a rule, the adenitis develops on the side of the lesion; exceptionally the inflammation may involve the glands of the opposite side.

Practically all chancroids are accompanied by an inflammatory enlargement of one or more lymphatic glands which become moderately tender on pressure and cause slight pain in walking. This inflammation usually subsides under rest and appropriate local treatment. In its more pronounced form one gland becomes so large, tender, and painful that there is serious interference with locomotion. This inflammatory swelling may subside under treatment or may be steadily progressive, may be accompanied by edema, widespread swelling, redness of the skin, one or more areas of softening, necrosis of the skin, and the discharge of pus. Under such circumstances the inflammation, at first confined to the gland, has involved the periglandular structures, the gland capsule having ruptured. This is characterized by a rather sudden subsidence of the severe and constant pain which accompanies these buboes, and is followed by more or less widespread tissue necrosis.

The pus discharged from these broken-down buboes may or may not be sterile. It does not contain the chancroidal bacillus nor are the resulting sinuses and ulcers likely to take on chancroidal action, except as the result of infection from without. In cases of glandular suppuration secondary to chancroid there are usually a number of glands involved; indeed, all the lymphatics of the inguinal region. The amount of necrosis, however, varies greatly; some glands may be completely broken down, others only partially destroyed. The latter may be the cause of burrowing sinuses which may persist for months.

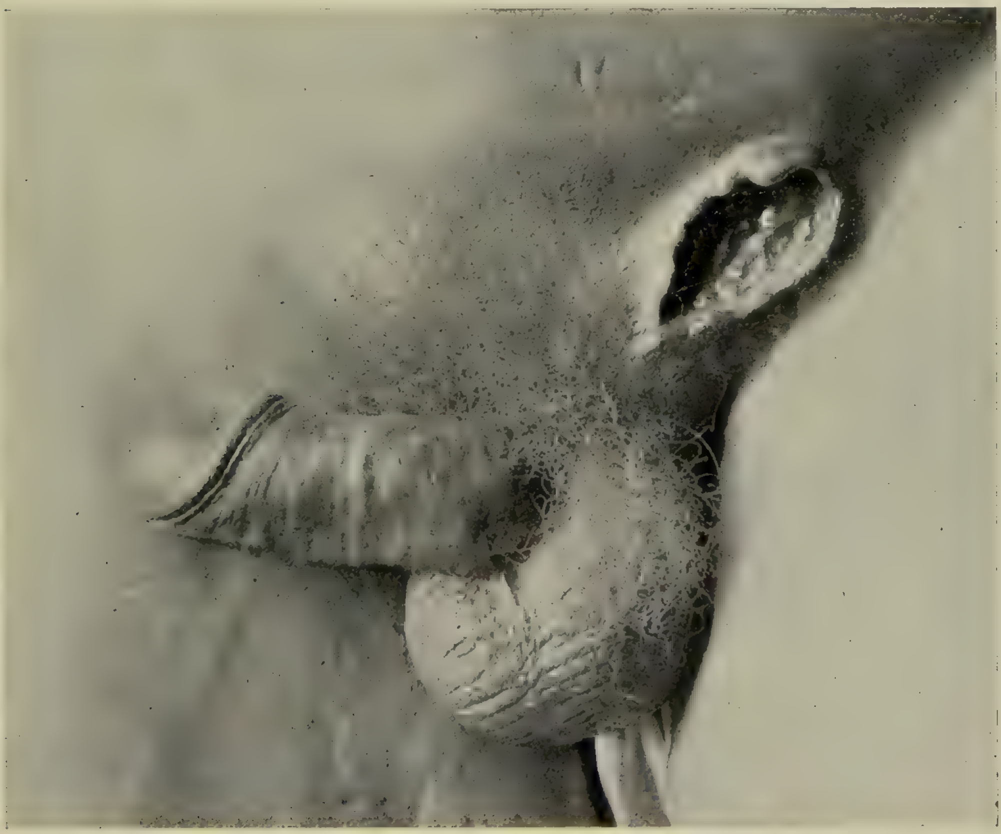


FIG. 169.—CHANCROIDAL BUBO (White and Martin).

As to the diagnosis of chancroidal bubo, it has at times been confounded with incarcerated hernia. The history of the latter affection should suggest its true nature.

Treatment of Chancroid.—The prophylaxis of chancroid is comparatively simple. This is especially true if only such lesions as are acquired during sexual congress are given this name. It should be remembered that pyogenic infection of the genitalia of those in a profoundly depressed condition may result in lesions so like chancroid, following so closely the clinical course of these sores, and even proving so abundantly auto-inoculable, that there is some reason on the side of those who hold that there is no such distinct entity as chancroid. It certainly lies in the experience of most surgeons to have observed chancroidal lesions on the sexual organs of those who have had no illicit intercourse. As a rule, however, and one to which there are few exceptions, the true chancroid is acquired by inoculation during sexual congress.

Unlike the manifestations of syphilis, those of chancroid are so acutely inflammatory in character and so conspicuous that, as a rule, it is difficult to overlook them even on casual inspection. It thus happens that among the intelligent and those of cleanly habits chancroid is a rare affection, and even among the lowly and ignorant it is found, as a rule, only in those who combine alcoholic with venereal excess. It is probable that infection is always accomplished through an abrasion or a skin lesion. There is also evidence to show that prompt antiseptic cleansing of abrasions which have been inoculated with chancroidal virus prevents the development of the lesion.

The treatment of chancroid when it has developed will depend to a large extent upon the character, number, and distribution of the lesions and upon the period of development at which they are seen. When the chancroid is observed within the first twelve hours of its development, it may be quite impossible to distinguish it from a simple infection. If, however, such a lesion, though it has been kept clean and free from mechanical irritation, has a distinct red areola and clearly punched-out border, and presents a gray sloughing surface, it is wise to regard it as chancroidal in nature and immediately to apply the appropriate treatment. If these features are not sufficiently well marked, a wet dressing should be applied for twelve to eighteen hours, the patient being given a bottle of dilute lead water and told to keep the gauze or cotton compress placed over the small lesion constantly wet. Simple infection is promptly bettered as the result of this treatment, while the chancroid will steadily, and sometimes rapidly, extend.

The treatment applicable to all undoubted chancroids seen in their early stage is complete and efficient cauterization or excision. The latter treatment is applicable only to chancroids placed upon the inner or outer preputial surfaces or the penile or scrotal skin.

If cauterization be inadequately applied it is worse than useless, adds greatly to the inflammatory edema, and encourages the subsequent spread of the infection. When skilfully used it at once converts the chancroidal ulcer into a simple sore, greatly lessens the dangers of complicating buboes, and is followed by healing in about a week.

The procedure may be rendered painless by local anesthesia and is best carried out by thoroughly cleansing the entire penis, first with soap and water, then with bichlorid 1:1000, and finally with sterile water. Thereafter there is sprayed with some violence directly against the ulcerated surface a 10 per cent. solution of cocain. The penis is again washed with soap and water and bichlorid, the chancroids are thoroughly cauterized by pure carbolic acid applied by means of cotton wrapped tightly about the end of a wooden toothpick or a split match. It is important that the carbolic acid be carried to every part of the chancroidal lesion and that it be prevented from reaching the surrounding healthy skin. In one minute the carbolic acid is neutralized by absolute alcohol applied on swabs to the burned lesions; thereupon the entire penis is swathed in a few layers of gauze, which are kept constantly wet with a mixture of dilute lead-water and dilute alcohol, equal parts of each. The cauterized areas, if they be within the preputial sac, are protected against the maceration incident to surface contact by small pledgets of cotton wet in the same solution, the latter being changed every time the patient urinates.

This carbolic cauterization is applicable to superficial chancroids, unless they be complicated by inflammatory swelling and edema so pronounced as to threaten the development of phimosis or paraphimosis. When the chancroid is deeper and more extensive, destruction of the specific lesion should be accomplished either by nitric acid or the actual cautery. The application of the former agent usually requires an anesthesia deeper than that practicable by cocain spray. This is particularly the case since the pseudomembranous coating of these deep ulcers is too thick to allow penetration of the anesthetic. Peripheral injections of eucain made by the hypodermic needle, however, will accomplish entire anesthesia. This, however, should not be made until the skin has been thoroughly cleansed. Nitric acid is applied on a swab and is rubbed thoroughly into every recess of the chancroid.

A better means of treatment is the actual cautery. The small point of a Paquelin cautery answers very well for this purpose, and when used should be carried not only into the obviously diseased tissues but a little beyond them in every direction. Otherwise the entirely cauterized area will be converted into a more virulent sore than that for which cauterization was practised. The use of the actual cautery should be preceded by thorough surgical cleansing of the healthy tissue surrounding the ulcers, and should be followed by the alcohol-lead-water wet dressing.

When the chancroid is seen in its very beginning, even if the diagnosis cannot be formulated, but is merely a matter of strong suspicion, and if the lesion be situated on the foreskin, it is best treated by excision. This should be preceded by thorough surgical cleansing of the surrounding area and injection of a few drops of eucain solution ($\frac{1}{5}$ of 1 per cent.) beneath and around the lesion. The small sore is then cauterized by carbolic acid, picked up in a pair of tooth forceps, cut out by means of scissors, and the resultant wound closed by suture. Thereafter surgical cleansing of the area involved should be repeated. If the sore is placed upon the glans or in such position that its excision implies resulting deformity, cauterization is indicated.

Where cauterization of the chancroid is not applicable because of objection on the part of the patient, or because conditions are such that the extensive application of the cauterant required for complete destruction of the sore is likely to be followed by inflammatory phimosis, the most efficient conservative treatment lies in the constant application to the chancroidal surfaces of a wet, mildly antiseptic dressing, such, for instance, as cotton moistened with dilute lead-water, protargol 1:1000, or boric acid 2 per cent. solution. The dressing in the case of small lesions placed beneath the prepuce which can be retracted is easily accomplished by spreading over the ulcerated surfaces a thin layer of dry cotton, which is then moistened with the solution of choice. The foreskin is drawn forward, the dressing being thus retained, preventing the maceration incident to apposed mucous surfaces. The patient is given a bottle of solution and is instructed to change his dressing each time he urinates or even oftener. When the chancroid is so placed that the dressing cannot be thus retained, gauze may be employed, which can be held in place by a few turns of a roller bandage or by a jock-strap.

When at the time the chancroid is seen it is large in area, inflammatory in type, and accompanied by great edema, the patient should be put to bed, should have his bowels freely opened, and should be given a light diet. The sore itself should be wet dressed, and preferably with a mild antiseptic solution. For the relief of congestion and edema gauze wrung out of a solution of ammonium sulphichthyolate 1:1000 answers admirably, the parts being elevated and the sore being cleansed every two hours by means of a spray of hydrogen peroxid one-half strength, followed by protargol 1:2000.

Chancroid complicated by phimosis may be treated by subpreputial irrigations of protargol, repeated every two hours night and day; the penis in the meantime being kept swathed in gauze constantly wet with lead-water and alcohol. If in spite of this treatment edema is steadily progressive, operation is indicated. This becomes imperative if the amount of inflammatory swelling is so great as to threaten gangrene. In preparation for operation the preputial sac is irrigated as thoroughly as possible with green soap and hot water, which is in turn followed by bichlorid solution 1:1000. The entire penis is cleansed with the same solutions as for any surgical operation. The prepuce is then split along the back to within a quarter of an inch of its attachment in the coronary sulcus and the raw surfaces left by the cut are at once cauterized with a hot iron, as are all the thus exposed chancroids to their deepest recesses. The penis, glans, and prepuce are again washed with soap and water and bichlorid solution, and are wrapped in gauze which is kept wet with lead-water and alcohol. The infiltration is usually so extensive as to make the performance of a circumcision inadvisable; indeed, it may be so great that a single dorsal incision will obviously be inadequate for the complete exposure of the lesions. Under such circumstances a cut should be made on each side from the preputial orifice to the coronary sulcus. After healing of the chancroids a satisfactory circumcision can be performed.

Paraphimosis should be relieved by freely cutting the constricting band and reducing. This operation should, however, be preceded by a thorough cleansing of the entire operative area followed by a most searching cauterization of the chancroids and of the incision required for reduction.

Gangrene is, as a rule, a sequel of phimosis or paraphimosis. It is best stayed by operations having for their object the relief of these conditions. When it occurs as the result of mechanical or chemical irritation or profound dyscrasia, it is best treated by hot applications in the form of gauze pads wrung out of a solution of mercuric chlorid 1:10,000, these compresses being changed every ten to fifteen minutes. Sitz baths lasting eight to sixteen hours, of bichlorid solution 1:40,000, are extremely serviceable. These should be combined with appropriate constitutional treatment.

For the slowly spreading destructive chancroids forming the so-called serpiginous ulcers and developing, as a rule, in the groins as a result of chancroidal infection of suppurating buboes, constitutional treatment is of prime importance. These cases are so often manifestations of late syphilitic infection that mercury and the iodids, when the kidneys are healthy, should be given one thorough trial. As a rule, tonic and stimulating treatment is distinctly indicated. Locally applications other than the actual cautery seem to be quite futile. The best results are obtained by prolonged baths of mild antiseptic solutions, preferably bichlorid of mercury or boric acid, these lasting for days or weeks.

Lymphangitis as expressed in the form of buboes is best avoided by keeping the ulcer clean and well drained and the patient quiet. It may complicate insignificant lesions, and is often, if not always, a result of inadequate drainage. It is frequently noted in such sores as are treated by dusting-powders other than iodoform, which, if this method of drug application is to be adopted for chancroid, is far more efficient than any of its substitutes.

One of the important reasons for the early excision or cauterization of chancroid is incident to the fact that such treatment, when successful, practically always prevents the development of chancroidal buboes. When the glandular inflammation is in its early stages,—*i. e.*, when it is characterized by the formation of one or more tender, movable, painful nodules in the groin,—it can usually be aborted by putting the patient to bed, opening his bowels freely, thoroughly cleansing and draining the chancroidal area by wet dressings frequently changed, and applying over the inflamed glands compresses wrung out of 1:1000 ichthyol solution fastened in place by a rather firmly applied spica bandage and covered by a hot-water bag. If after twenty-four hours of this treatment there is no improvement, time will be saved by prompt excision of all the affected glands, the most scrupulous care being taken during the operation to protect the wound against direct infection with the chancroidal virus. After removal of the glands the operative wound is closed without drainage and heals by first intention.

In case this formal operation should not be feasible, each enlarged gland should be injected with 5 to 20 minims of a 3 per cent. solution of carbolic acid, this being driven directly into the center of the gland, after which compresses wrung out of ichthyol are placed over the region of inflammation and kept in place by a spica bandage. Fresh ichthyol solution is poured on these compresses, keeping them constantly wet. These carbolic injections frequently but not always prevent the buboes from breaking down and forming abscesses.

If when the patient is seen there is an inflammatory tumor which on palpation shows distinct evidence of softening, the overlying skin is carefully cleansed as for surgical operation. With a tenotome the abscess cavity is punctured and the contained pus is evacuated through this small opening, after which a 10 per cent. iodoform-glycerin solution is driven in by means of a syringe with a small nozzle until the abscess cavity becomes tense. A dressing of gauze wrung out in 1 : 10,000 bichlorid is then held in place by a spica bandage. If there be a re-accumulation of fluid in the abscess cavity it is again evacuated, the treatment being repeated twice. Thereafter if there be no betterment the abscess should be opened freely, thoroughly curetted, all surrounding enlarged glands should be removed, and the resulting wound should be partly closed by suture, packed with sterile gauze, and covered in by an antiseptic dressing.

If when the case first comes under observation there are abscess formations, with the overlying skin thin, blue, and discolored or already ruptured, the groin should be opened freely and all diseased glands should be removed either by dissection, if they are not completely broken down, or by curetting, and the resulting wound should be partly sutured and packed with sterile gauze.

If when the patient is first seen there is a history of suppurating buboes which have been opened, and from the incision of which pus continues to be discharged, and if on examination there are found burrowing sinuses leading to other enlarged glands, a free opening of all the sinuses and complete removal by dissection of all diseased glands is the only successful means of treatment, since the sinuses continue to discharge because of necrotic material which will require months for spontaneous extrusion.

The records of clinical cases show that the operation for removal of diseased inguinal and femoral glands is not absolutely free from danger. Aside from the complications incident to all wounds and the subsequent development of elephantiasis of the penis and scrotum, there is danger of converting the entire incision into a huge chancroid. The femoral glands when inflamed may contract close adhesions to the femoral vein. Thus it has happened many times that in removing these glands the femoral vein has been torn, resulting always in alarming hemorrhage and occasionally in death from gangrene, due, as a rule, to simultaneous ligation of both the femoral vein and artery for the control of hemorrhage. If in the course of operating for pus such an accident as a rupture or tear of the vein should occur, the wound in the vessel should be plugged, the vein should be freely exposed above and below by careful dissection, should be lightly clamped, and the rent in its lumen should be closed by suture.

CHAPTER XX.

SYPHILIS.

By Edward Martin, M.D.,

PHILADELPHIA.

Syphilis is a disease due to a specific microörganism and transmissible both by inoculation and heredity.

Except in its hereditary and maternal forms syphilis first develops as a local sore, usually single, indurated and chronic in type, appearing about three weeks after inoculation (the period of primary incubation).

This is followed in one or two weeks by enlargement of those lymphatic glands into which pass the lymph-vessels from the seat of this sore; and in the course of the next four to six weeks (the period of secondary incubation) by enlargement of all the lymphatic glands of the body, associated with diminution in hemoglobin, slight leukocytosis, fever, rheumatoid pains, and eruptions upon the skin and mucous membranes.

These in turn are followed in the course of one or many years (the intermediate period) by round-celled infiltrations which may involve any of the tissues of the body and which exhibit special predilection for the vessels, bones and periosteum, and the nervous system. The infiltrate may be diffuse or circumscribed, in the latter cases forming distinct tumors called gummata.

History of Syphilis.—It is the commonly accepted belief that when Columbus discovered America his sailors contracted syphilis from the Indians, carrying to Europe a disease hitherto unknown.

Against this belief Hirsch has advanced strong arguments showing that syphilis was recognized at a much earlier period even in Europe, and others have apparently proved that in the writings of the Chinese more than 2000 B. C. unmistakable descriptions of this disease are to be found. It was not, however, generally recognized by the medical men of Europe until the end of the fifteenth century, when, because of its virulence and wide diffusion, it was extensively studied and accurately described. The virulence and mortality dependent on this epidemic strongly suggest that it was then developing at the expense of a non-immunized and hence highly susceptible population.

At the present day syphilis has practically spread over the entire world, and nearly everywhere appears in a type so mild as to suggest a partial hereditary immunity, though doubtless the comparative innocuousness of the disease as it now appears should in some measure be attributed to a more rational treatment.

Cause of Syphilis.—The evidence as to the microbian origin of syphilis is overwhelming, yet it must be confessed that the specific microbe has not yet been conclusively demonstrated. Though a number of bacteria have been isolated from the discharges or scrapings of syphilitic lesions, none has stood the test required before a microörganism can be conclusively proved to be the causative factor of a given disease: that is, none have been isolated, grown in pure cultures, and caused syphilis by inoculation of such pure culture. Until comparatively recent times none of the bacteria described as specific to the affection could be habitually recovered from even the primary and secondary lesions.

The most promising studies in this direction are those concerning the Treponema (Spirochæta) pallidum. This was first noted as a habitual organism of primary specific lesions by Schaudinn and Hoffmann, and has subsequently been found by Metchnikoff, Roux, Rosenberger, Flexner, and many other thoroughly competent observers. It is an actively motile spirillum, hard to find even in fresh lesions, and not readily stained. It varies in length from 4 to 14 microns, in width from an immeasurable thinness to 0.5 of a micron, has from 3 to 12 curves and pointed ends. It has been found only in syphilitic lesions, and has been usually prepared from the scrapings of chancres, enlarged glands, mucous patches, and flat condylomata.

The Treponema pallidum is best stained with Giemsa's azure-eosin mixture applied for from one to twenty-four hours. The material to be examined is spread upon a cover-glass or a slide, is fixed in absolute alcohol for ten or twenty minutes, and the stain is then applied. It is difficult to see the organism and the study of several of the spreads may be needful before its presence is demonstrated. As a rule, two or three of the spirilla are present in the field of the microscope. Twice this number of the Spirochæta refringens may be visible, but these are not characteristic of specific lesions.

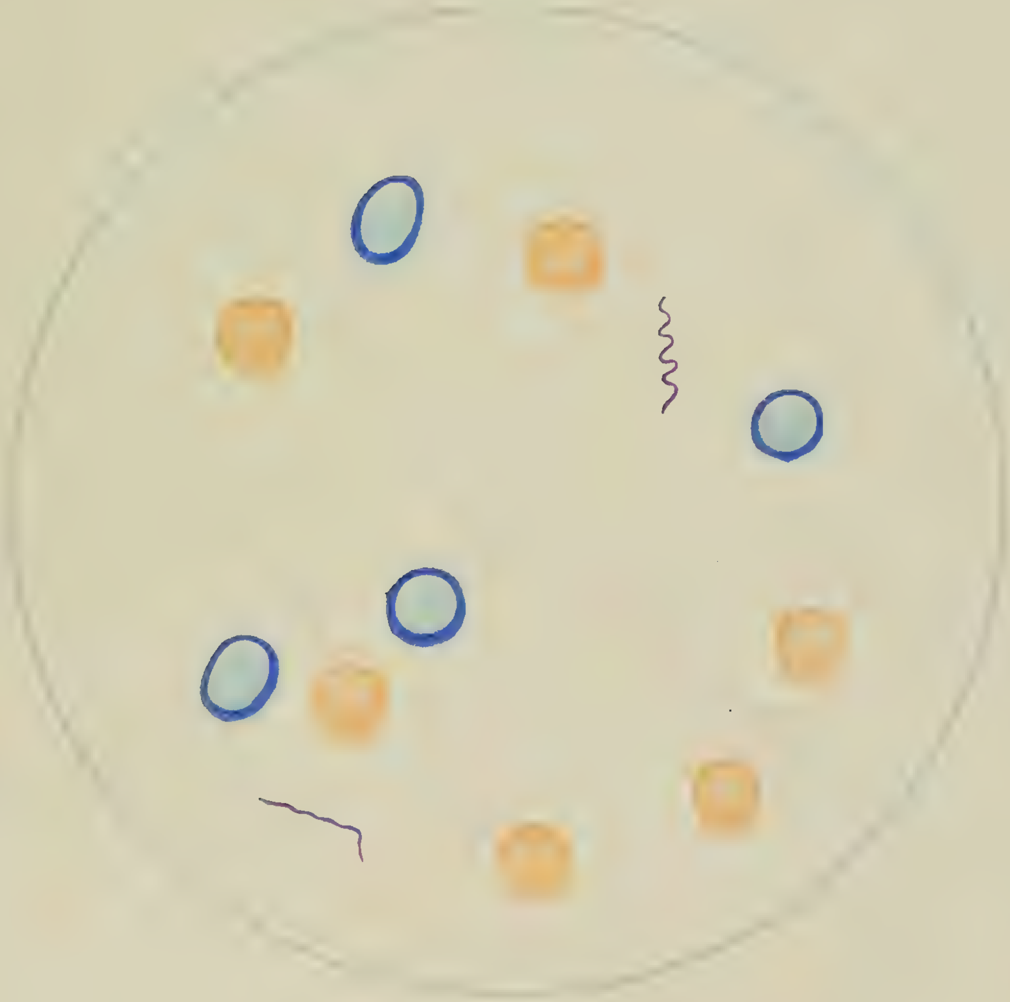
Types of Syphilis.—Syphilis may be spontaneously aborted or abortive, benign with but a single outbreak of constitutional symptoms or occasional recurrent superficial transitory outbreaks, remittent with repeated and persisting early and late lesions, or malignant.

The aborted or abortive type of syphilis is an unusual form of the disease in which the chancre is not followed by skin and mucous membrane eruptions nor by appreciable signs of specific fever or cachexia. The disease may end with a chancre being entirely aborted, the tissue resistance being sufficient to overcome the infection. Or in the abortive form it may become latent, gummatous infiltration involving the deeper structures not developing till years later. Thus there is a type of syphilis without secondaries, even though no treatment be given.

The benign type of the disease, the one commonly encountered, is that in which about six weeks after the appearance of a chancre there is an eruption upon the skin and mucous membrane preceded by slight fever, moderate anemia, and non-crippling rheumatism. This eruption quickly fades under treatment and never reappears, nor do tertiaries develop.

A variation of this type, equally common, is characterized by one outbreak of syphilitic rash accompanied by mucous membrane lesions

PLATE XV.



TREPONEMA PALLIDUM (White and Martin).
(Preparation and drawing by Randle C. Rosenberger, M. D.)

which subside under treatment; later from time to time there is a recurrence of mucous patches in the mouth and throat and more rarely papular or papulo-pustular eruption.

The remittent type is characterized by frequently repeated outbreaks in both the early and late stages of the disease, the lesions often yielding slowly to treatment. There is generally an associated systemic depression.

The malignant type is characterized by an outbreak of eruption, pustular almost from the first, and pronounced lesions of the mucous membrane. These both persist and recur and are likely to be associated with deep ulcerative and destructive lesions even in the early course of the disease. This type is commonly observed in those who are excessive in the use of alcohol or tobacco or who have crippled kidneys and are thus unable to take adequate doses of mercury.

As to the prognosis, from the standpoint of the type of the disease an early outbreak of pustular manifestations and the precocious development of the deep and destructive lesions of the late period threaten not only function but life itself.

Immunity against late lesions is not foreshadowed by the mildness of the early constitutional symptoms, possibly because these are not treated with the same vigor and fidelity that is accorded to the more obstinate types.

Transmission of Syphilis.—Syphilis may be transmitted: (1) To any non-immunized person by inoculation with the discharges from any of the lesions of a person exhibiting the early stages of the disease (within two years from the appearance of the chancre). The blood also may transmit the infecting microörganisms during this period. (2) To the embryo by the spermatozoa of a syphilitic father or through the blood of a mother suffering from the disease. (3) To the mother through the placental circulation of a child syphilitic by the spermatozoa of an infected father.

The body secretions of a syphilitic, such as the milk, saliva, tears, and sweat, will not convey the disease unless they are mixed with the discharge of an ulcerating lesion. This suggests a filtration action of the secreting cells by means of which the specific mircoörganism is retained in the system. This is also true of the semen, which, while incapable of being successfully inoculated, may carry to the ovum an infection which will result in typical manifestations of hereditary syphilis.

The transmissibility of the disease by inoculation is in inverse proportion to its age. An active mercurial treatment distinctly shortens this period, and after two years the blood and discharges are not inoculable, though transmission to offspring is still possible.

The conditions necessary for the development of a chancre, the first lesion of syphilis, are the contact of syphilitic blood or discharges with a wound or abrasion of a non-immunized person.

Direct or mediate contagion is the term applied to the method of transmission when it is incident to the bodily contact of a person free from syphilis with another exhibiting the primary or secondary lesions of the disease. It usually takes place during sexual intercourse, and through surface breaks or abrasions so slight as to escape notice at the time. It sometimes results from ardent kissing, from bites, or, in the case of physicians, from the physical examination of syphilitic patients. Exceptionally it has followed the perfunctory family salute.

The inoculation of a chancre upon the nipple of a healthy woman as the result of suckling a syphilitic child has in the past been so common as to have suggested legislation for its prevention.

Syphilis insontium is a term applied to the disease when it is acquired in ways other than those incident to the sexual approach or its perverted manifestations. Except that the chancre is usually extragenital, the disease runs the same course as when acquired in the usual way.

Indirect or mediate contagion is the term applied to the method of transmission by which there is no direct surface contact between the giver and the receiver of the disease, but the virus is carried through the agency of an intermediate body. Under this heading would properly come those cases in which syphilis is contracted from a strumpet, herself free of the disease; the virus under such circumstances having been deposited by a syphilitic man but failing to inoculate the woman because she is either immune or exhibits no mucous membrane lesion. This form of transmission, though rare, undoubtedly occurs, and it is quite possible thus to transmit the disease to a woman through the agency of a man who remains healthy.

Indirect transmission is usually accomplished by means of pipes, cigars, razors, styptic alum sticks, brushes, combs, cups, knives, spoons, glasses—indeed, any of the instruments and utensils used in common by a number of persons without proper cleansing between each use. Both surgical and dental instruments have thus carried contagion, and there can be no question but that it may be conveyed by towels, sheets, pillow-cases, and articles of clothing.

When vaccination was commonly practised with scabs derived from those previously vaccinated, the conveyance of syphilis by this means, though rare, was observed in a sufficient number of cases to cast great discredit upon this preventive treatment of smallpox.

Hereditary transmission may be from the father or the mother or both. It is possible for the child to be born of a syphilitic father and subsequently exhibit the characteristic symptoms of secondary syphilis, the mother remaining entirely free from such symptoms and nursing this child without contracting chancre. More commonly she acquires the disease from the infected fetus through the placental circulation, in which case it may assume a latent form.

Periods of Syphilis.—On the basis of the clinical course of the disease syphilis in its symptomatology and evolution is classified as follows:

The period of primary incubation. The time elapsing between inoculation and the appearance of the chancre will average three weeks.

The period of secondary incubation. The time elapsing from the appearance of the chancre to the development of cutaneous and mucous membrane lesions will average six weeks.

The secondary period, usually two years, during which time the early or secondary lesions are prone to appear.

The intermediate period, usually one year, varying from this time to thirty years; the intervals during which time lesions are absent.

The tertiary period, beginning usually three years from the time of the initial lesion and lasting indefinitely. During this period gummata develop.

Individual cases in their evolution by no means correspond to this scheme. Deep, infiltrating, destructive lesions often develop early, even within a few months of the appearance of a chancre, or eruptions of the secondary type may appear years after the original infection. Moreover, in cases treated carefully and vigorously from the beginning there will be no manifestations of the disease either in the secondary or tertiary periods, while in cases irregularly treated or receiving no medication there may be no intermediate period, the gummatous lesions directly succeeding those more superficially placed.

Perhaps one reason for this chronologic classification is the generally accepted doctrine that syphilis is transmissible solely during the secondary period. Finger holds that tertiary processes are due to the action of toxins which manifest a predilection for the system showing the least resistance, and are distinctly predisposed to by trauma. Thus late cerebral syphilis is commonest in brain-workers and hepatic syphilis in drinkers, while gummata most frequently involve those bones subject to repeated injury.

There are apparently well-authenticated cases to show that syphilis may be transmissible for many years. Thus, Fournier and Feulard have noted such cases, and Tarnowsky states that the disease is contagious for fifteen years.

The non-heredity of the tertiary period shows some exceptions; thus, Feulard records the fact that a syphilitic father procreated four healthy children but transmitted his disease to the fifth.

The tertiary phenomena are favored by inadequate treatment, by excessive alcoholism, and by infection in a climate different from the one to which the inoculated subject is accustomed. Moreover, persons exhibiting an idiosyncrasy against mercury or suffering from visceral disease are specially prone to tertiary lesions.

Immunity Against Syphilis.—*Acquired Immunity.*—Those who have contracted syphilis either by heredity or contagion are immune against a further inoculation of the disease. A few carefully observed cases prove that this law has an occasional exception.

Hereditary Immunity (Profeta's Immunity).—Children born of syphilitic parents but failing to exhibit signs or symptoms of the disease are for a time immune against inoculation. This period of immunity is often transitory, since cases have been reported of chancre and secondaries in the young children of a mother suffering from tertiary symptoms. Moreover, E. Fournier and Jullien have recorded many cases of the acquired disease in those born of syphilitic parents and exhibiting the dystrophic and nutritional changes incident to syphilotoxins.

Maternal Immunity (Colles's Immunity).—Mothers of children syphilitic by the spermatozoa of the father are immune against contracting the disease by inoculation, being able to nurse children exhibiting secondary lesions of the mouth without fear of developing chancre. It is probable that this immunity is due to the fact that the mother has already acquired the disease through the placental circulation—though the symptoms may be wanting.

There is no race nor individual immunity aside from the forms of the latter just described.

PARASYPHILIS.

Under this term, first popularized by Fournier, are grouped affections which follow syphilis and are predisposed to because of it, but which are not benefited by antisyphilitic treatment. Indeed, they are usually made worse.

These parasyphilitic affections are expressed in a variety of ways upon the skin and mucous membrane. Leukoderma, which develops rapidly in the course of two or three weeks without symptoms, forming irregular gray, yellow, or brown spots, geographic in outline, sometimes appears upon the neck and shoulders of women. Its duration and time of appearance are uncertain. Keloid, forming distinct encapsulated tumors, may grow about the cicatrices of former syphilides. Onycholysis (loosening of the nails) is common in old people and may be syphilitic or parasyphilitic. The same is true of clavi forming in the palms of the hands and the soles of the feet.

In the mouth pityriasis and leukoplakia are common, appearing in the form of gray patches on the cheek, lips, tongue, or tonsils. Ultimately they become fissured and papillomatous, and in tobacco-users and those past middle life may be transformed into cancer.

Tuberculosis, amyloid degeneration, saccharine diabetes, endarteritis, functional neuroses, and neurasthenia are often secondary to syphilis. Headache is the commonest parasyphilitic phenomenon. Pain is usually in the occipital region, is dull, often attended by backache and tenderness along the spine.

Vasomotor and trophic disturbances are frequent, exhibited by pallor or flushing with marked interference with reflexes, malnutrition, anemia, dry shedding hair, urticaria, herpes, feeble heart action, gastro-intestinal atony, and sexual debility.

Tabes gives a syphilitic history in 70 to 90 per cent. of cases. General paralysis is due to syphilis in 90 per cent. of cases; epilepsy and progressive muscular atrophy frequently follow syphilis. Infantalism, hydrocephalus hare-lip and cleft palate, club-foot, idiocy, any of the dystrophies, may be parasyphilitic in nature.

THE CHANCRE.

With the exception of the hereditary form of the disease and that acquired by the mother from a fetus syphilitic by the spermatozoa of the father, a chancre is the primary lesion of syphilis. This is the first demonstrable sign of infection, commonly appearing as a trifling abrasion which becomes slowly and painlessly larger and is circumscribed by a characteristic induration. By the time this induration becomes obvious to physical examination the perivascular lymph spaces are found gorged with small round-celled exudate wide of the original lesion.

In the first few days of its development the chancre presents no feature which enables it to be distinguished from an abraded or herpetic spot. It appears as a small, red, varnished, slightly oozing, indefinitely circumscribed superficial lesion absolutely indistinguishable from similar non-specific sores. The raw surface is often covered by a gray, boggy pseudo-membrane. The sore in its development becomes rounded and indurated and usually remains superficial; when depressed it assumes a cup shape with regular sloping borders.

Induration is the most characteristic feature of the chancre, surrounding the ulcerating lesion in the form of a disk which can be definitely outlined on palpation. The disk-like induration varies in apparent thickness from that of a sheet of parchment to that of a blotting-pad. In palpating for this the sore is lightly grasped and lifted up by the finger and thumb of the examining surgeon. The induration of a sore upon the foreskin is best demonstrated by stripping the latter back; in the course of the stripping the infiltrated portion will project as would a plate of cartilage beneath the skin.

The induration of the chancre persists for from one to six months after the ulcer is healed. Since the ulceration of chancre is at the expense of the infiltrate, the scars are either trifling or entirely absent.

Chancre has certain peculiarities which when they are all present enable the diagnosis to be made with considerable certainty even in the absence of a history of exposure to infection. Its characteristic features are:

(1) A period of incubation varying from twelve to fifty days but averaging three weeks. Between the date of inoculation and the development of the primary lesion of syphilis there is a period of absolute latency in so far as symptoms are concerned.

(2) The sore is distinctly indolent. It is attended by little discomfort, discharges but moderately, and is usually covered by a grayish pellicle.

(3) It is rounded in form.

(4) It is indurated. This induration may precede ulceration. It commonly becomes marked in from five to seven days after the sore has developed. It varies greatly in its extent, being especially marked upon the genitalia of the male, and often being quite absent when a chancre develops on the vulva or vagina. As a rule, extragenital chancres exhibit an induration more inflammatory in type than that which characterizes the genital lesion of the male type.

(5) It is accompanied by painless enlargement of the lymphatic glands which receive the lymph-vessels from the surface upon which the chancre is placed. Except there be mixed infection these glands are hyperplastic rather than inflammatory in type, and when the receiving glands are grouped more than one are affected. In the case of genital or anal

chancre one to two or three of the inguinal glands on each side of the body will be enlarged to about the size of the last joint of the little finger.

(6) It is persistent in spite of local treatment. Ordinary cleansing applications are quite without effect and it remains either stationary or slowly progressive for weeks.

(7) In the light of recent researches the scrapings of the sore may be expected to show the presence of the Spirochæta pallidum.

(8) It promptly heals as the result of constitutional treatment by mercury.

(9) It is single in about 80 per cent. of cases.

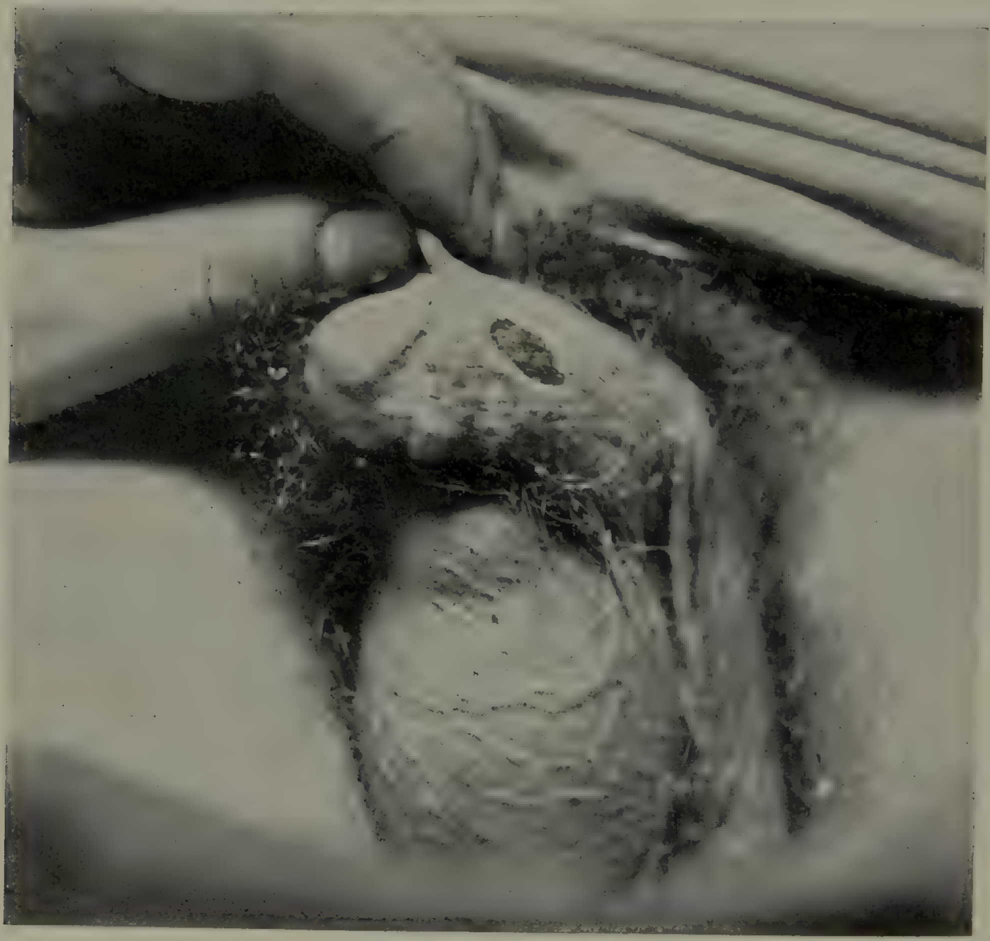


FIG. 170.—CHANCRE.

Genital chancre usually appears as a single sore, placed in or behind the coronary sulcus, on the glans penis, about the frenum, or on the preputial margin. It may be found anywhere on the skin of the penis (Fig. 170) or scrotum.

The ulceration may remain superficial, constituting a chancrous erosion. It may be moderate in depth, constituting the chancrous ulceration, or it may be quite absent, the lesion then remaining as an indurated papule. Erosion and ulceration are the common types.

There are departures from these types which may be deceiving. The lesion sometimes begins as a "silvery spot" placed on the surface of the glans, ultimately breaking down in the form of a chancrous erosion. It may begin as a typical herpes, with multiple lesions, due probably to specific inoculation of herpetic raw surfaces, and is to be distinguished from the latter only by persistence and characteristic evolution. These lesions form the multiple herpetiform chancre.

The Hunterian chancre is an ulceration characterized by the depth of the lesion and usually the extent and hardness of the induration.

The mixed chancre, that is, a lesion in which the chancroidal virus has been inoculated, together with that of syphilis, may not be recognized until the development of secondary symptoms points conclusively to constitutional infection. The acute inflammation attending chancroid may entirely mask the characteristic induration of the chancre. The persistence of an indolent indurated ulceration attended by characteristic adenopathy should suggest this form of chancre.

The chancrous erosion is the form in which the initial lesion develops in about two-thirds of all cases. It begins much as a slight scratch or abrasion, differing from the latter by the persistence of the lesion or lesions under ordinary cleanly treatment, by the fact that they tend to become oval or rounded, that they are surrounded by a dusky areola presenting a raw surface, the center of which is covered by a thin pseudo-membrane, and which gives a moderate discharge of blood-stained serum. The characteristic induration develops in five to seven days and the glandular infiltration in about twice this time. The lesion remains superficial and usually leaves no scar, thus differing from a chancrous ulceration, in which there is destruction not only of the infiltrate but of the tissues of the part.

The indurated papule in which no ulceration takes place, and which may appear simply in the form of a small, hard, dusky red tubercle, sharply defined by the surrounding tissues, constitutes a primary lesion so inconspicuous that it is usually not recognized until secondary symptoms suggest a search for the seat of original infection. Fortunately, this form of infection is extremely rare.

One other rare form of primary infection may appear in the form of a syphilitic balano-posthitis, the specific nature of which is suggested not so much by the appearance of the lesion as by the initial degree of induration, and the indolence and persistence of the lesions. This also is an extremely rare form of primary infection.

The meatal chancre is fairly common; it forms a deep ulcer attended by pronounced inflammatory swelling. This ulcer is usually irregular in outline and quite atypical. It is differentiated from chancroid by the fact of its slow progression and its marked infiltration. Moreover, the characteristic inguinal adenopathy develops early. Chancroid in this region is rapidly destructive.

The diagnosis of chancre of the urethra is difficult mainly because the presence of this lesion in such a position is not suspected. It is usually situated within half an inch of the meatus. Exceptionally it has been observed as far back as 1½ inches. A urethral discharge appearing more than fifteen days after exposure should always suggest a search for urethral chancre. It is usually mistaken for a mild gonorrhea complicated by folliculitis.

The characteristic symptoms are a moderate blood-stained discharge, ardor urinæ, distorted stream or slow dribbling urination, induration, and marked edema of the frenum. The adenopathy is early and characteristic. Examination with a short urethroscope shows a rounded, somewhat elevated, superficial area of ulceration.

Genital chancres of women are, as a rule, but slightly indurated. They develop usually on the labia majora or minora and are common in the region of the fourchette and clitoris. They are very rarely observed on the surface of the vagina, but are sometimes seen about the os uteri, and present in general the rounded shape and the indolent ulceration of chancre elsewhere. Those involving the external genitalia are accompanied by inguinal adenitis, and this is also true of chancre about the anal region.

Chancre of the os must be distinguished from ulcerating folliculitis, mechanical erosion, herpes, and malignant growth. Ulcerative folliculitis exhibits, as a general rule, small multiple lesions which are associated with chronic catarrhal conditions and heal promptly under treatment. This is also true of herpetic lesions, while mechanical erosions disappear on removal of the cause. The diagnosis of chancre from cancer is usually obvious, but at times must be formulated from the slow and inevitable progression of the latter.

Extragenital chancre is scarcely susceptible of being classed under headings based on anatomic conformation. These lesions vary extraordinarily in size, configuration, depth, and degree of concomitant inflammation. They have perhaps but one common characteristic—the lesion persists in spite of treatment and slowly extends for several weeks. It is accompanied, as a rule, by pronounced enlargement of the associated lymphatic glands, it is more inflammatory in type than the genital lesions, and is sometimes extremely painful.

The ordinary seats of the extragenital chancre are the lips, the tongue, the nipple, the anal region, and the fingers.

That extragenital chancres, are not, as a rule, recognized as such in their early stages is sufficiently attested by the fact that the diagnosis is rarely formulated until the outbreak of secondary symptoms. The very fact of these lesions not being placed upon the genitalia prevents them, as a rule, from being subject to inspection of those most skilled in their detection. The extragenital lesion is nearly always single, and only in exceptional instances can a clear history of exposure to syphilis be elicited. The period of incubation is about the same as that which obtains in the case of genital chancres. As a rule, the lesion exhibits the characteristics which mark it in its usual site. But it may depart so widely from this type as to make a diagnosis based on inspection impossible. Thus a genital chancre, as a rule, does not exceed the size of a 10-cent piece. The extragenital lesion, particularly as it occurs upon the face, may be larger than a dollar. Inflammatory phenomena are commonly more marked in the extragenital lesions, and the accompanying adenitis is often of a mixed type, *i. e.*, the glands cannot be felt as distinct painless nodules, but are more likely to form a merged tumor.

On general principles all lesions, whether they be upon the face, lips, mucous membrane of the mouth or hands, which develop without apparent cause, persist for weeks in spite of appropriate treatment, and are accompanied by marked adenopathy, should excite suspicion.

On the head and face the common causes of chancre are to be found in razor-cuts, scratches, or exceptionally superficial bites which, having healed, reopen in the course of two or three weeks and persist as ulcerating surfaces which become rounded in form and crusted and discharge a blood-stained serum. Cracks and fissures about the nose and mouth develop into chancres in a similar way. Surrounding the lesions there is usually an area of inflammatory edema, and with but few exceptions there will be developed in the course of two weeks a distinct enlargement of the lymphatic glands of the neck. If the chancre develops upon the scalp or in the beard, it closely simulates ecthyma. The history of its development, beginning as an indurated papule or erosion, and the subsequent development of symptoms, will determine the diagnosis.

Chancre of the eyelid is usually mistaken for a stye. In its earliest manifestations a distinction between these two affections may be impossible. The development of an indurated erosion or ulceration should in a few days suggest the diagnosis. Lymphatic enlargement incident to chancre in this position is first observed in the glands in front of the ear and near the angle of the jaw.

It is particularly on the head and face that chancre is likely to attain enormous dimensions, to be inflammatory in type, and to be without obvious characteristic induration. Under such circumstances, aside from the causelessness and persistence of the lesion and glandular involvement, there will be nothing to suggest the diagnosis until blood changes and secondary lesions throw light on the affection. Given a suspicion as to the nature of the lesion, the prompt effect of mercuric treatment would be of distinct diagnostic value.

Chancre of the lip commonly begins as a fissure or erosion such as commonly follows herpetic ulceration on the burn of a pipe or cigarette. In this stage of development the diagnosis is absolutely impossible unless further search prove that a detection of the spirochæta pallida derived from scrapings is a practical procedure.

The ordinary erosions of the lip reach their maximum in two or three days and promptly subside, being cured in at most a week or ten days. The chancre, however, develops progressively, producing a large distinct and rounded ulcer, the mucous surface of which is covered by a dirty gray pseudo-membrane, the skin surface by a black scab. It is surrounded by an area of inflammatory induration and accompanied within two weeks by enlargement of the submental lymphatic glands. The inflammatory edema involves, as a rule, the entire lip, producing a conspicuous deformity and simulating closely a well-developed epithelioma. Indeed, excision has more than once been practised because of a mistake in diagnosis. The rapidity of development should render this error a most unlikely one.

Chancre of the tongue is commonly observed on the dorsal surface of the anterior half of this organ or on the borders or tip. It produces a painless oval or rounded lesion, placed upon an elevated area of induration, often covered by a pseudo-membrane (Plate XVI, Fig. 1). The glands most frequently involved are the suprahyoid and the submental, though Fournier notes that in chancre of the tip glandular enlargement is noted just behind the symphysis.

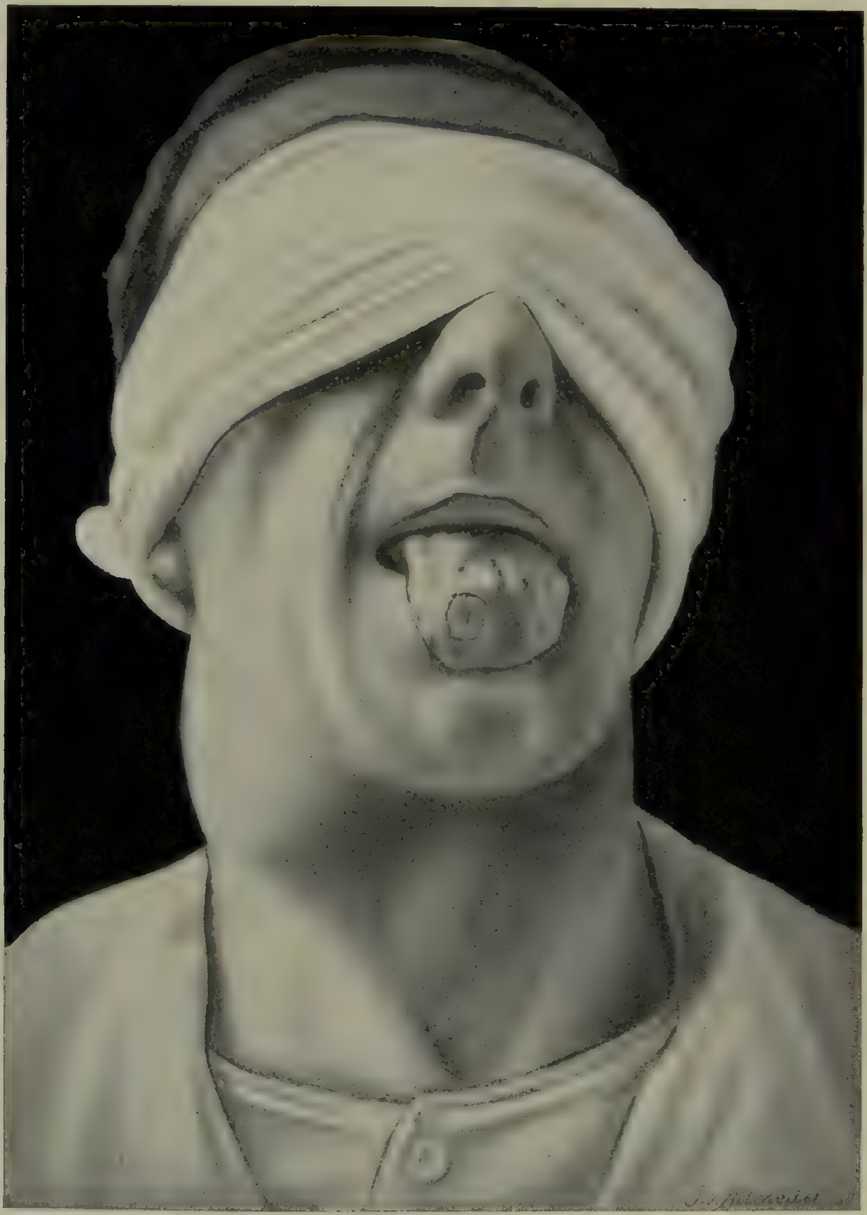


FIG. 171.—TYPICAL CHANCRE OF THE TONGUE, SHOWING ENLARGEMENT OF THE ANATOMICALLY ASSOCIATED LYMPHATIC GLANDS OF THE NECK.
Duration two weeks. Incubation three weeks.

There is a deep form of lingual chancre characterized by large size, pronounced induration, and depth of ulceration.

Lingual chancre in its early stages so exactly simulates the common lesions of the tongue that a differential diagnosis is not possible. It is

PLATE XVI.

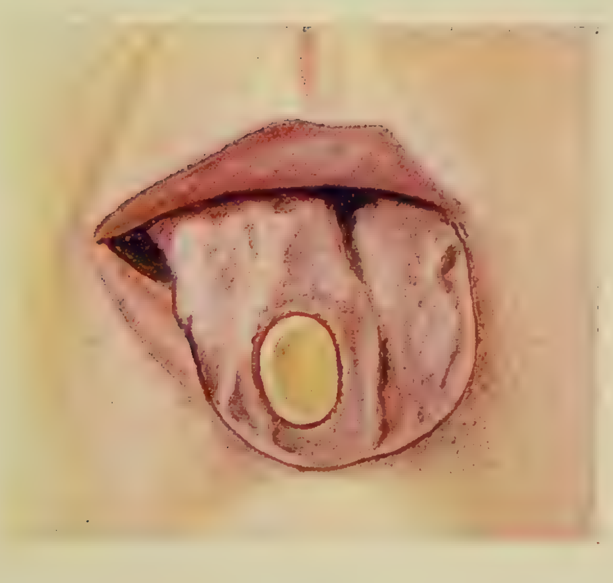


FIG. 1.—CHANCRE OF THE TONGUE TWO WEEKS OLD.

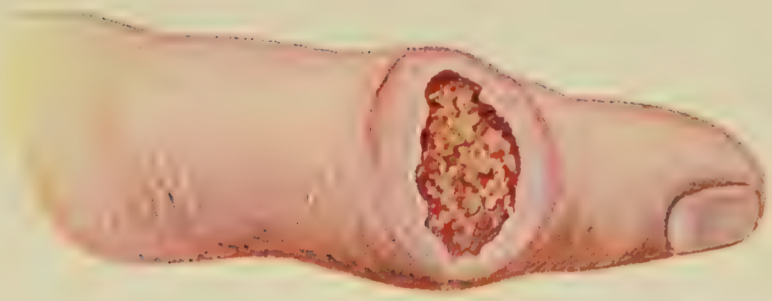


FIG. 2.—CHANCRE OF THE FINGER FOUR WEEKS OLD.

only by the persistence of the lesion, its fairly rapid extension, the surrounding induration, and the glandular involvement that the true nature of the affection is determined.

As is the case with labial chancre, an early diagnosis is particularly important, since the lesion in this region is most likely to carry contagion to the innocent.

Chancre of the tonsil or of the fauces is, as a rule, not recognized as such until secondary symptoms develop. It is characterized by ulceration, covered by pseudo-membrane, sometimes superficial, resembling a mucous patch, sometimes deep and destructive, this being particularly the case when the tonsil is affected (Plate XVII). The parotid lymphatic glands are involved early and extensively. Again, the diagnosis must be based on the apparent causelessness of the lesion, its persistence and extension in spite of local treatment, lymphatic enlargement, and the prompt effect of specific medication. As a rule, patients thus afflicted do not present themselves for treatment until the secondaries are well developed. It will then be found that there is a history of prolonged and persistent sore throat, associated with swelling of the neck.

Chancre of the breast is, as a rule, observed in women, and is incident to suckling syphilitic infants. There are some cases reported in men. The lesion is usually placed on the nipple or at its base, and simulates in its early development a simple fissure or erosion.

The diagnosis is not made until the lesion, by its persistence, extent, configuration, and associated lymphatic enlargement, demonstrates the fact that it is more than a simple infection. When chancres appear upon the skin overlying the breast, they exhibit much the same appearance as similar lesions upon the genitalia.

Chancre of the anus is more commonly observed in women because the infection is with them readily carried by discharges trickling down from the vagina and thus inoculating cracks or fissures which may exist in the anal region. The lesion in its first development is often linear, since the area of inoculation has probably been a lesion of similar shape. This linear ulceration persists, gives a thin blood-stained discharge, is comparatively painless, and is attended by inguinal adenopathy. Typical rounded chancre sometimes develops. The diagnosis will be suggested by the causelessness and persistence of these lesions and the associated typical inguinal adenopathy.

Digital chancres commonly develop at the edges of the base of the nails, the inoculation having been received through abrasions or surface breaks in this region. They start as apparently causeless erosions, papules, or pustules which are shortly accompanied by so much swelling of the digital pulp as to suggest the development of a felon. The progression of the lesion is slow, a matter of days rather than of hours, is accompanied by pain which is moderate in intensity as compared with that of a felon, is characterized by superficial ulceration (Plate XVI, Fig. 2) with but little discharge, is uninfluenced by local treatment, and is shortly followed by epitrochlear or axillary enlargement; the former in case the ring or little finger is enlarged, the latter if the thumb, index, or middle finger is affected. The lesion at times appears as a simple papule, which is so small and excites so little attention that it is ignored until the development of secondaries.

The digital inoculation of syphilis and septic infection at the same time is characterized by the acute local and general symptoms of the latter, followed by a persistence of the lesion resulting from the incision, curetting, and cauterization practised for the relief of the acute infection. The ulcerating surface shows no tendency to heal, is often persistently and distressingly painful, and is not recognized as syphilitic till constitutional symptoms develop, since the specific adenopathy is usually masked by the glandular enlargement incident to the pyogenic infection.

The Diagnosis of Chancre.—Although a typical chancre presents features which when associated are in themselves almost diagnostic, it must be confessed that even those most experienced will often hesitate to formulate the positive diagnosis of syphilis on a primary lesion. Some specialists still hold that the diagnosis is assured only by the appearance of secondary manifestations. Such practice ignores the type of syphilis unaccompanied by early constitutional symptoms.

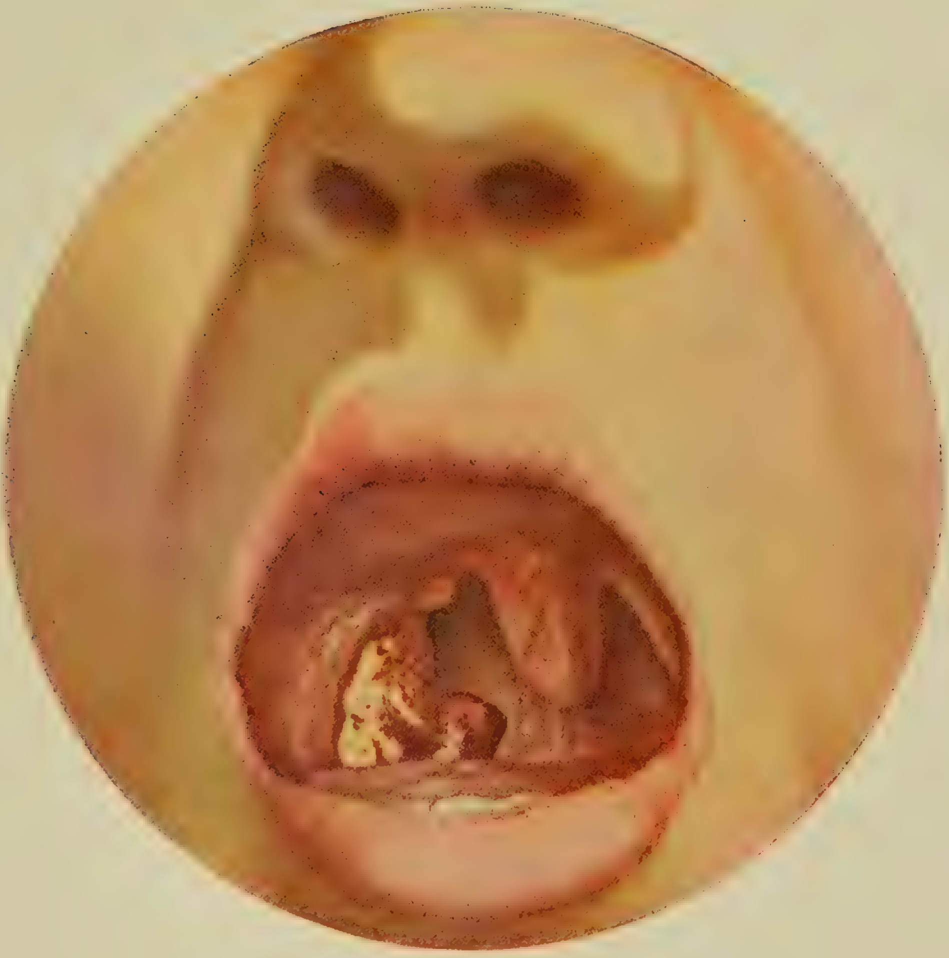
If it be held that the treatment of syphilis should be delayed until the secondary rash has developed, or completely omitted should this not appear, the early diagnosis is of no importance except from the standpoint of taking measures against the transmission of the disease. For those, however, who believe that syphilis is most effectively treated by excision of the chancre and the institution of a vigorous antispecific treatment at the earliest possible time, the prompt recognition of the syphilitic nature of the sore is of great importance.

Whether the primary lesion be genital or extragenital, single or multiple, typical or atypical, the diagnostic features on which greatest reliance is placed are: (1) A period of incubation, not less than ten days, usually three weeks; (2) induration; (3) slow extension and painless persistence of a sore which remains rounded; (4) painless, non-sensitive enlargement of the anatomically associated lymphatic glands. All these features are present in the great majority of primary lesions. All may be absent and may remain so until unmistakable secondaries demonstrate the true nature of the infection.

The period of long incubation if it can be definitely established, especially if it is corroborated by a confrontation, is in itself almost diagnostic. But such a history is rarely obtainable. There have usually been one or more exposures following that in which infection was acquired, or there has been trauma, such as a riding-chafe, sufficient to explain the development of the atypical excoriation. A persistent, slowly spreading ulceration, exhibiting a tendency to become rounded in form, may occur from a simple infection in those who are uncleanly in their habits or who subject abrasions to recurring trauma, though in either case the lesion is apt to be more irregular in outline and more inflammatory in type than is characteristic of a chancre.

Almost painless, slightly tender, polyganglionic lymphadenitis is a common accompaniment of genital herpes. When it is remembered

PLATE XVII.



Syphilitic Chancre of the Tonsil (Diphtheroid Form) (Fournier).

that a multiple chancre has been called herpetiform because it so closely resembles the latter lesion, it can readily be seen that the difficulties in diagnosis on first inspection may be great. The herpetiform chancres, however, are persistent, do not appear in successive crops, and become to some extent indurated, while the adenitis is slowly progressive and much more marked than is common in simple herpes. It is characteristic of multiple chancres that they develop at or about the same time, not following each other by a perceptible interval, exhibit each during the course of several weeks about the same stage of evolution, and are not auto-inoculable, though prolonged contact of the moist secreting surface of the chancre with a tender skin, such as the scrotum, may produce a simple sore on the latter.

When the initial lesion appears as a balanoposthitis the diagnosis cannot be made until the persistence of the lesions, the distinct infiltration, and the inguinal enlargements suggest that there is an underlying condition infinitely more serious than that incident to simple purulent infection.

Any non-syphilitic sore (and this is particularly true of chancroid which has been treated by repeated applications of caustics) may exhibit the typical induration of chancre, and in persons of low vitality or uncleanly habits may be extremely slow in healing. Indeed, the diagnosis of genital sores which have been cauterized is quite impossible except from their evolution.

Perhaps the greatest difficulty in the examination of a sore itself will be encountered in distinguishing between the primary chancre and the so-called chancre redux or relapsing chancre, which is in reality a gumma implanted upon the seat of primary lesion. This gumma begins as an infiltrate which breaks down, forming a deep ulcer surrounded by dense walls. It is distinguished from chancre by the history of the case and by the absence of the typical enlargement of the associated lymphatic glands.

Finally, it must be borne in mind that the glands which receive the lymph-vessels from the surface on which the chancre is placed may show no palpable change, or through mixed infection may suppurate. The superficial glands are so often enlarged through causes other than syhpilitic infection that the tumefaction must have followed the latter by the usual interval, to be of diagnostic value.

The diagnosis of mixed chancre, that is, of a lesion due to infection both of chancroidal virus and that of syphilis, must be based on a knowledge of the history of the case and prolonged observation. If a chancroid and syphilis be acquired at the same exposure, the former will have developed and run through its contagious course before the symptoms of the latter begin. If in two or three weeks the chancroid which has not been cauterized develops marked induration followed by a polyganglionic, painless enlargement of associated lymphatic glands a chancre should be suspected. A chancroidal lesion more commonly develops on the seat of a beginning chancre. In this case the ulcerating destructive sore absolutely conceals the true nature of the original lesion, and it is not until the outbreak of secondary symptoms that the specific nature of the infection is recognized.

Although a typical chancroid can be recognized as such, it is never safe absolutely to assure a patient that there is not also engrafted upon this lesion the poison of syphilis. These mixed sores are fortunately rare.

GENERAL SYPHILITIC INFECTION.

Following the appearance and development of the chancre and the syphilitic buboes there is a period of latency, called the period of secondary incubation, during which the infection is being disseminated.

The manifestations of general infection are alterations in the blood, enlargement of lymphatic glands not in immediate relation with the chancre-area, neuralgic or rheumatic pains, impairment of nutrition with or without fever, accompanied by eruptions on the skin and mucous membranes, and involvement of the bones, joints, and tendinous sheaths, or the viscera.

Alterations in the Blood.—It is probable that blood alterations have already begun by the time a typical chancre is developed; they are not, as a rule, demonstrable for about four weeks from this period or two weeks before the outbreak of skin and mucous membrane lesions. There will then be noted a diminution in hemoglobin and in the total number of red corpuscles, together with a slight leukocytosis. These changes are, as a rule, moderate in degree, and are not invariably present, though they are sufficiently common to constitute a valuable diagnostic symptom in conjunction with the preceding history.

The test sometimes described as the Justus test, in accordance with which twelve hours after the inunction of a dram of mercuric ointment there should be a pronounced reduction of hemoglobin, is without diagnostic value.

The blood alterations are, in general, such as are characteristic of infectious diseases, and are less marked than those accompanying acute infections because of the probably slow multiplication and diffusion of the germ.

Impairment of the General Health.—Beginning about the fourth week from the appearance of chancre, when the blood changes become demonstrable, there is often an apparently causeless impairment in health, characterized by lassitude and loss of color and weight; with this condition may be associated anorexia and dyspepsia. Exceptionally there is a ravenous appetite. These symptoms are in the majority of cases so slight as to be elicited only on close questioning. They are at times so well marked that it is for this condition rather than the presence of a local sore that the physician is consulted.

Fever.—In the fifth week of the development of the chancre this failure of health may be associated with moderate fever, remittent in type, with evening exacerbations, as a rule so slight as to be noticed only when the patient is under medical observation, sometimes so pronounced that a typhoid condition is suspected. Murchison, Jenner, Musser, Baumler, and others have called attention to fever in the later stages of syphilis. Musser states that fever, either continuous or intermittent, is an expression of the activity of the syphilitic process, and that in obscure cases its presence with other symptoms is corroborative of this specific infective process.

When the fever is high and continued, running 103° and upward, is associated with severe bone pains and followed by a pustular eruption, it so closely simulates smallpox that an error in diagnosis is readily made.

Rheumatism.—Associated with the fever and malaise, or in the absence of these, patients from the fourth to the sixth week from the appearance of the chancre complain of pain which they variously describe as neuralgic or rheumatic. These pains are commonly referred to the region of the neck or the shoulders. They may occur in any part of the body and exceptionally are so severe that when associated with hyperpyrexia they are mistaken for signs of acute inflammatory rheumatism. Since at this stage of the disease there is at times painful effusion into one or more joints, such a mistake in diagnosis may readily be made.

The pain of early constitutional syphilis is usually most severe at night. It may be accompanied by tenderness over the bones, particularly the middle third of the ribs and the lower third of the sternum, and exceptionally develops in connection with distinct nodes, generally found over the frontal or parietal bones, the tibia or shafts of other long bones.

The headache which sometimes precedes the development of secondaries may be agonizing in type, and, associated as it is frequently with nausea and giddiness, indicates acute meningeal congestion.

Among other symptoms preceding the eruptions of the skin and mucous membrane are jaundice, albuminuria, alterations of cutaneous sensibility, exaggerated reflexes, enlargement of the spleen and liver, and paralysis of the ocular muscles.

General Lymphatic Enlargement.—It is probable that all the lymphatic glands become enlarged as a result of systemic infection, though the group lying along the outer border of the trapezius and a single gland placed in front of the internal condyle of the humerus are the ones which most typically show the hard, painless, non-sensitive overgrowth which is characteristic of syphilis.

In the post-cervical group it is customary to find, perhaps a week before the skin eruption, one or two, sometimes an entire chain of hard nodules, at most not larger than the end of the little finger, usually one-fourth this size.

Absence of Prodromes.—In a fair proportion of cases none of these prodromal symptoms are observed, the patients maintaining their bodily weight, their normal activity, and their proper color until a general skin efflorescence denotes the presence of constitutional disease.

AFFECTIONS OF THE SKIN AND MUCOUS MEMBRANES.

The cutaneous and mucous membrane manifestations of systemic infection upon which the diagnosis of syphilis is usually made commonly develop about forty-two days from the appearance of the chancre. They have been observed as early as the fourteenth day and as late as the sixth month. Exceptionally they have failed to appear even in the absence of specific treatment.

Syphilitic skin lesions in the early part of the disease are, as a rule, superficial, and heal without scars, though at times there is left permanent pigmentation. Later, in the tertiary period, they are often deep, involving the true derm, and unless their resolution is accomplished before ulceration has taken place they are followed by permanent scars or pigmentation or both.

The presence of syphilis does not prevent the development of other skin diseases and may mimic with great fidelity almost any of the lesions of the latter. The eruption, however, during its early or secondary period is characterized by its slow and painless development, absence of itching, coppery or raw ham color, symmetric grouping, rounded form with tendency to scale, superficial character, and prompt yielding to mercurial treatment.

As the disease ages the lesions exhibit other characteristics which are regarded as peculiar to the late secondary, intermediate, or tertiary period. They appear in groups or clusters in certain parts of the body, often symmetrically placed on the two sides, but not as a general eruption. Each lesion is rounded in form, and when these lesions merge the outlines of the resulting sore are circinate. Dry lesions are covered with layers of gray adherent scales; ulcers appear as though punched out and are often covered with thick, black, laminated scabs. The lesions do not exhibit the local or constitutional symptoms of acute inflammation.

Syphilitic Skin Eruptions.—The cutaneous lesions of syphilis are classified in accordance with their appearance as: (1) Erythematous, (2) papular, (3) vesicular, (4) pustular, (5) pigmentary, (6) bullous, (7) tuberculous, (8) gummatous. This also constitutes a chronologic order of development, to which, however, there are so many exceptions as to make it of little practical service.

The lesions exhibit a dilatation of the blood-vessels with a thickening of their endothelium and a cellular infiltration of their adventitia. The tertiary lesions differ from the secondary only in the fact that the cellular infiltration is much more extensive, involving usually not only the entire skin-thickness, but also the subcutaneous tissues. Ulceration in these lesions is due to a cellular overcrowding so great as to cut off the nutrition of the central part, causing necrosis. This necrotic area may be absorbed without ulceration, resulting in the formation of sometimes deforming cicatrices. This is particularly the case in the internal organs.

Erythematous Syphilides.—The first skin eruption of syphilis is usually erythematous in character and is perhaps the most constant of all cutaneous manifestations of the acquired disease. It develops about six weeks from the appearance of the chancre and with subjective symptoms so entirely wanting that it may for some days escape the attention of the patient. In its early manifestation it presents a mottled appearance similar to that observed on delicate skins when a surface ordinarily protected is exposed to the cold. Nor may it pass beyond this development, provided treatment promptly be administered. Usually it is first observed on the flanks, chest, and abdomen, though the subsequent well-developed eruption may be most conspicuous at the hair-line of the forehead or upon the palms of the hands and the soles of the feet. Its development upon the extremities is less marked, but it sometimes appears as a universal eruption.

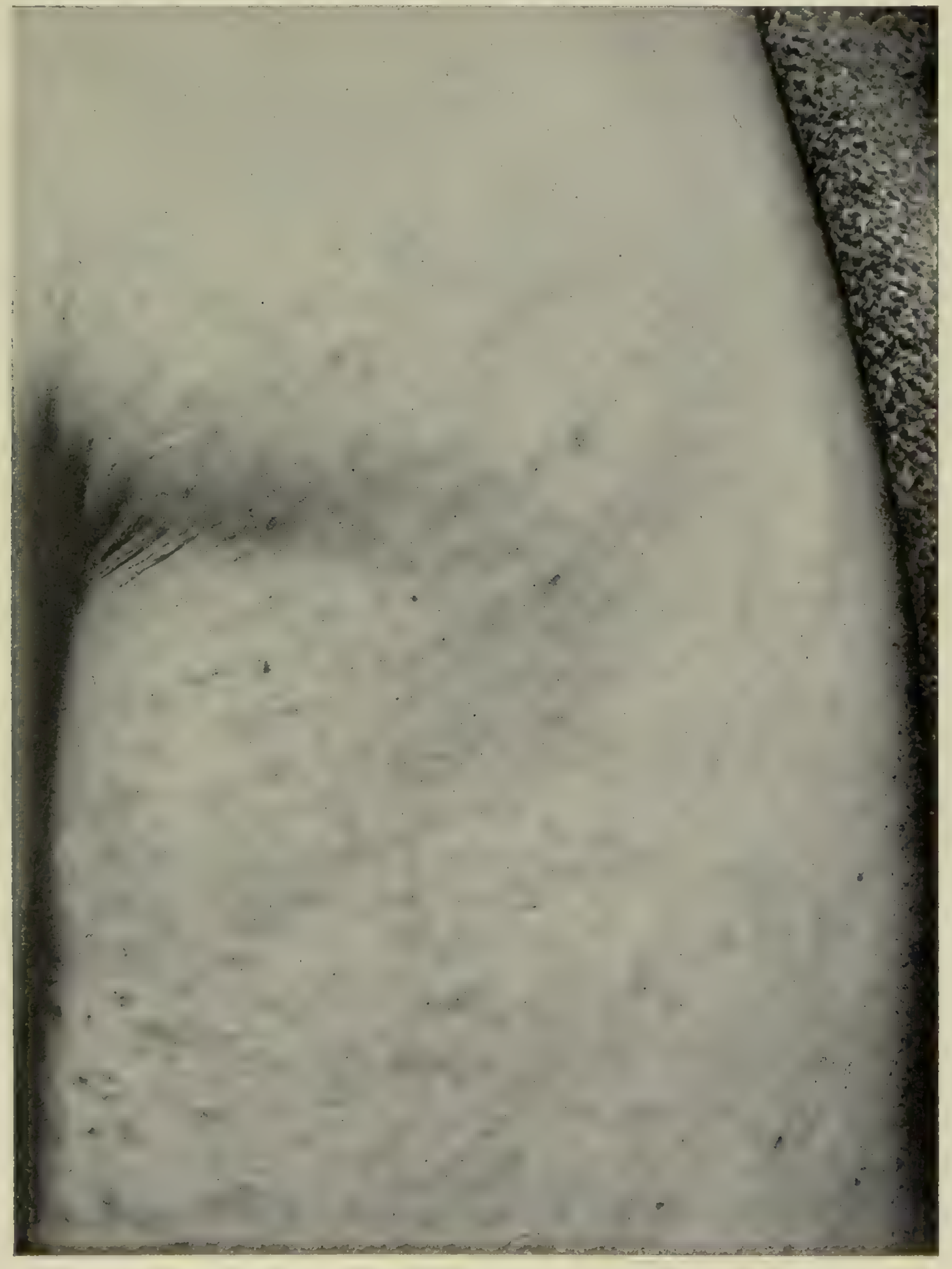


FIG. 172.—MACULO-PAPULAR SYPHILIDE.

This mottling is succeeded in a few days by a distinct macular eruption (Figs. 172, 173), rounded or irregular in form, the individual lesions varying greatly in size, shortly becoming raw ham or coppery in color, due to a distinct pigmentation, and not disappearing on pressure. It reaches its complete evolution in about a week, and under treatment usually disappears in a little longer time, though after the first three days of mercurial medication the individual lesions become slightly edematous and distinctly more marked. This is a sign of rapid resolution. If untreated the eruption persists until it is mixed with papules and pustules characteristic of the further evolution of the systemic disease (Fig. 174).

The *diagnosis* of the erythematous syphilides is based on the history of a preceding suspicious sore, attended by first local, then general, lymphatic enlargement, and other prodromes of syphilis; finally by the results of the therapeutic test. In its early stages it may be extremely difficult from inspection alone to distinguish this eruption from that due to copaiba, simple erythema, or measles. Pityriasis rosacea may so closely resemble the syphilitic eruption that with the preceding history

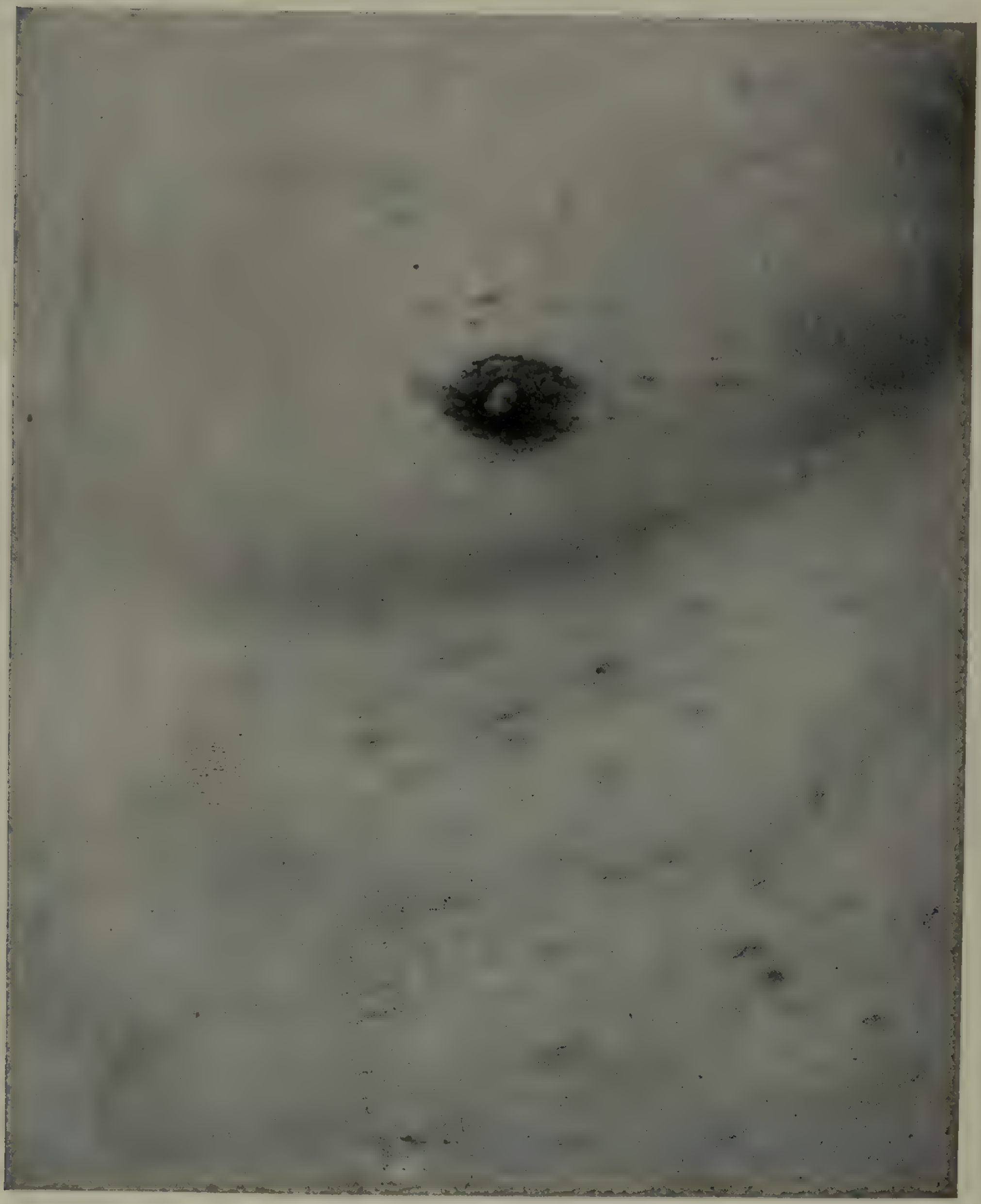


FIG. 173.—MACULAR SYPHILIDE.

of a suspicious sore a diagnosis may be quite impossible from inspection, and must be based on the therapeutic test, this disease having a tendency to persist for from one to three months.

The non-syphilitic erythema is usually caused by digestive disturbances and disappears rapidly under appropriate treatment. Measles even in its mild form has associated symptoms and runs an acute febrile course which makes the diagnosis clear.

Papular Syphilides.—Papular eruptions appear as hard, rounded elevations, varying greatly in size from that of a pin's head to that of the finger-nail. The surface of the papule may be conical or flat. It commonly exhibits scaling. The color is always a coppery red. This lesion, especially in the form of small papules, is commonly associated with the erythematous form. In grouping it is often circinate, and is characterized by the usual absence of subjective symptoms.

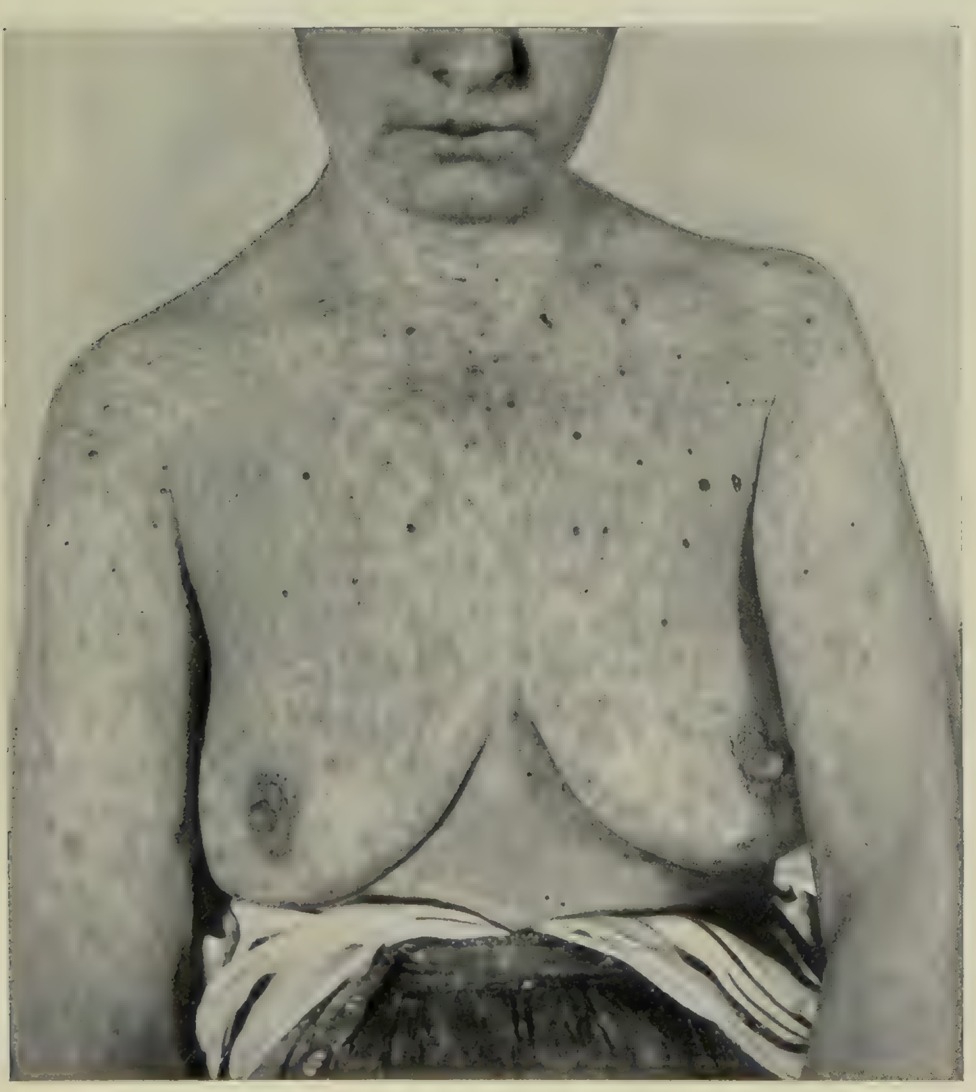


FIG. 174.—MACULO-PAPULO-PUSTULAR SYPHILIDE.

The small conical papules commonly appear on the face and afterward involve the rest of the body (Fig. 176). The small flat papules are noted first about the shoulders; afterward they may become general, being especially numerous on the flexor surfaces of the joints.

The large conical papules are usually discrete and comparatively few in number, being most abundant on the back, the buttocks, the back of the neck, and the anterior surface of the thighs.

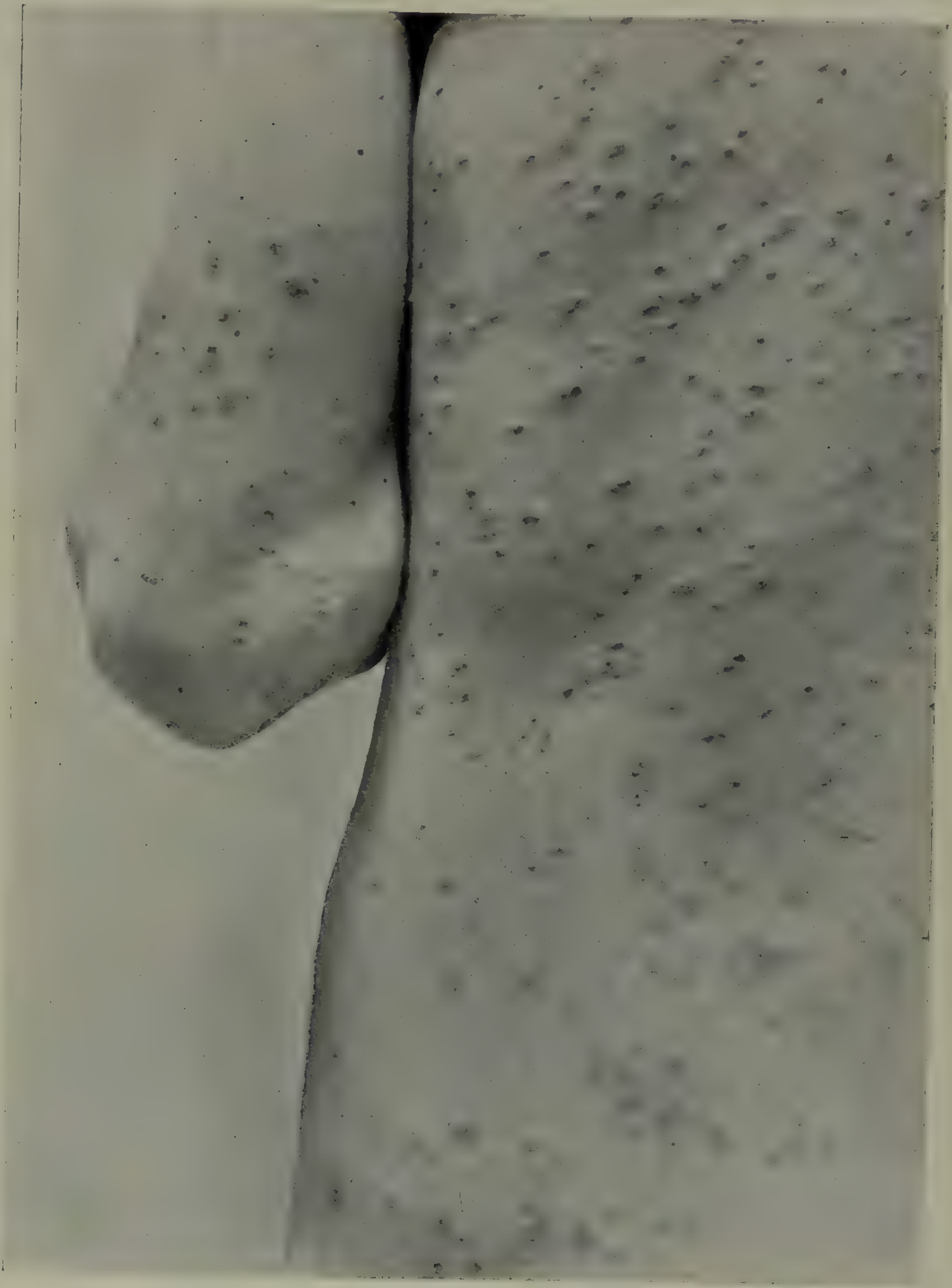


FIG. 175.—SMALL ACUMINATED PAPULAR SYPHILIDE.

The large flat papules may be discrete or grouped. They are perhaps commonest on the back, the nape of the neck, and the forehead. They are also observed on the flexor surfaces of the extremities, the scrotum, and about mucous outlets. In the latter case they are likely to become fissured or eroded. Indeed, whenever they are so placed that they are kept moist and chafed by skin-contact, as, for instance, when they are located upon the scrotum (Fig. 176), about the anus or the mucous surfaces at the corners of the mouth, within the buccal cavity, between the toes, or beneath the foreskin, the scaling which is characteristic of the lesions placed upon dry surfaces is replaced by a gray, pultaceous, ill-smelling pseudo-membrane (mucous patch). About the lesion, and caused either by irritating discharges or the syphilitic hyperemia, are often found distinct vegetations which may involve the surface of the lesion itself. These vegetations commonly present a smooth, raised, raw surface, the so-called condyloma lata or venereal wart. Exceptionally the papillomatous outgrowth may be so excessive as to cause cauliflower-like projections called vegetating papules (Fig. 177), common about mucous outlets, sometimes seen on the face or body.

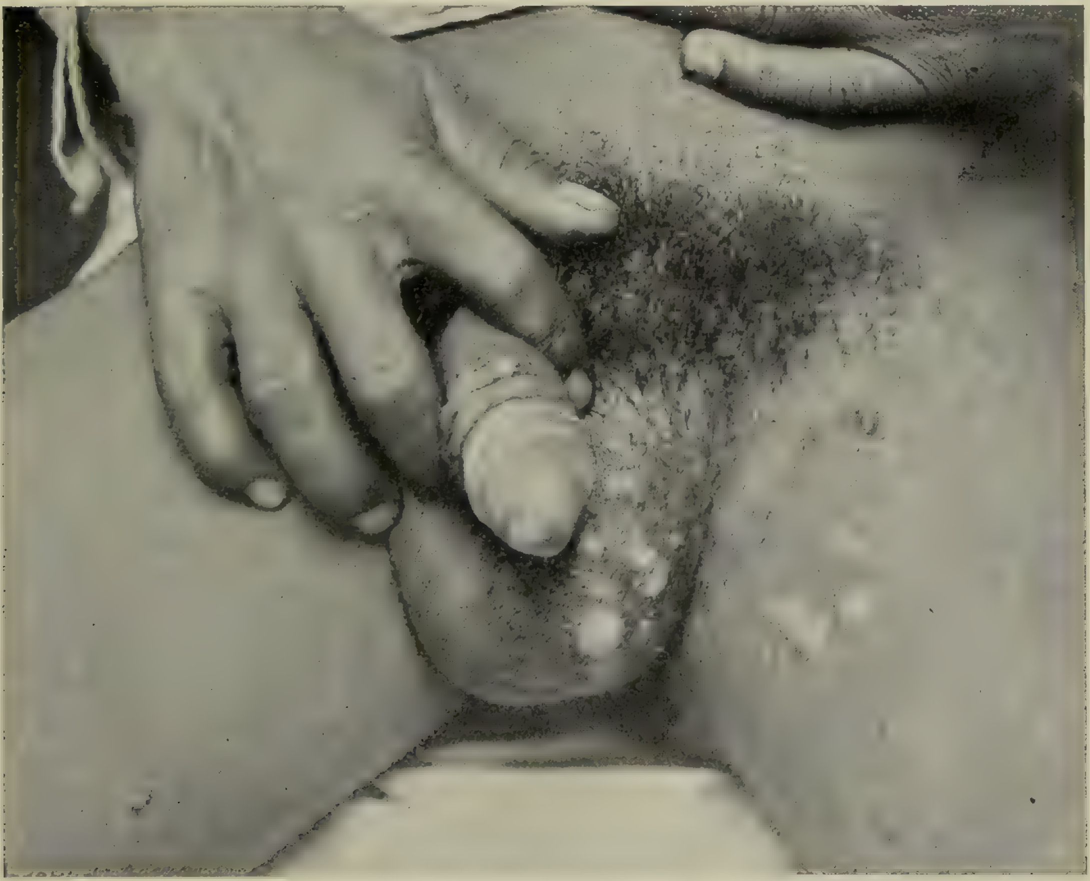


FIG. 176.—MUCOUS PATCHES (MOIST PAPULAR SYPHILIDE).

Because of the extreme delicacy of their skin and the friction and moisture to which it is subject in the natural creases, mucous patches are extremely common in syphilitic infants. The mucous patch is a flat papular eruption of syphilis, the surface of which has been macerated and eroded and is covered by a pseudo-membrane. It is common on mucous surfaces, but under favoring conditions develops on the skin.

The diagnosis of papular syphilis is based, in the main, on the concomitant signs of the disease, though the large flat papules are so characteristic as not to be mistaken for any other affection. The small papules closely simulate papular acne. The seat of predilection of the latter, however, namely, the forehead, chin, shoulders, and back, the absence of pigmentation, its long continuance and the scars of former lesions, usually suggest the true nature of the affection.

Lichen, though closely simulated by some of the flat papular syphilides, does not exhibit the circinate grouping of the latter, usually itches, and does not react to the therapeutic test. Moreover, the individual lesions are not distinctly rounded.

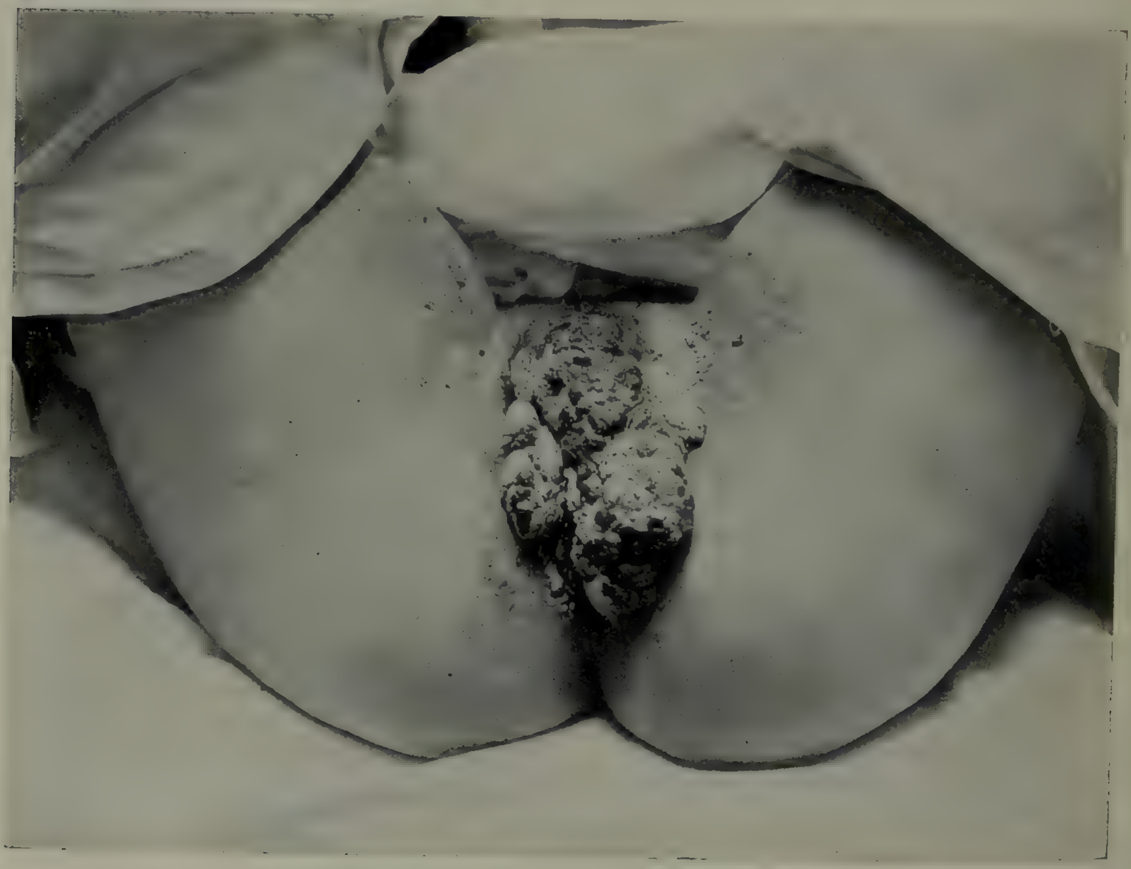


Fig. 177.—Vegetating Syphilide.

The papular syphilide yields to mercurial treatment in the course of weeks rather than days, and disappears without scar or pigmentation.

Papulosquamous Syphilide.—This lesion may appear either early in the course of constitutional syphilis or late in the disease. When it develops early it will appear after the sixth month of syphilis as a general eruption. It presents much the appearance of a papular syphilide, except that it is characterized by an abundant scaling which readily may be rubbed off, leaving a smooth, shining, copper-colored papule beneath. On the palms and soles these lesions are peculiarly persistent, and in place of appearing as rounded papules covered by easily detached scales they may develop as shot-like conical projections of hard, inspissated epithelium, which can be dug out from the skin, leaving distinct pits.

Painful fissures often complicate the papulosquamous syphilides of the feet. The lesions on the palms and soles may be discrete or confluent. At times on the palms the exfoliation becomes widespread, giving the surface of the skin a "silver" aspect. These lesions are highly characteristic of syphilis.

The diagnosis at times will have to be differentiated from psoriasis. This latter disease is rarely confined to the soles and palms, but invades by preference the extensor surfaces of the knees and elbows, remains as a scaling, superficial, symmetric eruption without a preceding history of syphilis, and is unaffected by mercurial treatment, though it must be remembered that the papulosquamous syphilide is extremely rebellious to medication. When the palmar and plantar syphilides become fissured and eroded the diagnosis is extremely difficult, and in the main will have to be based upon the history of the case and the therapeutic test.

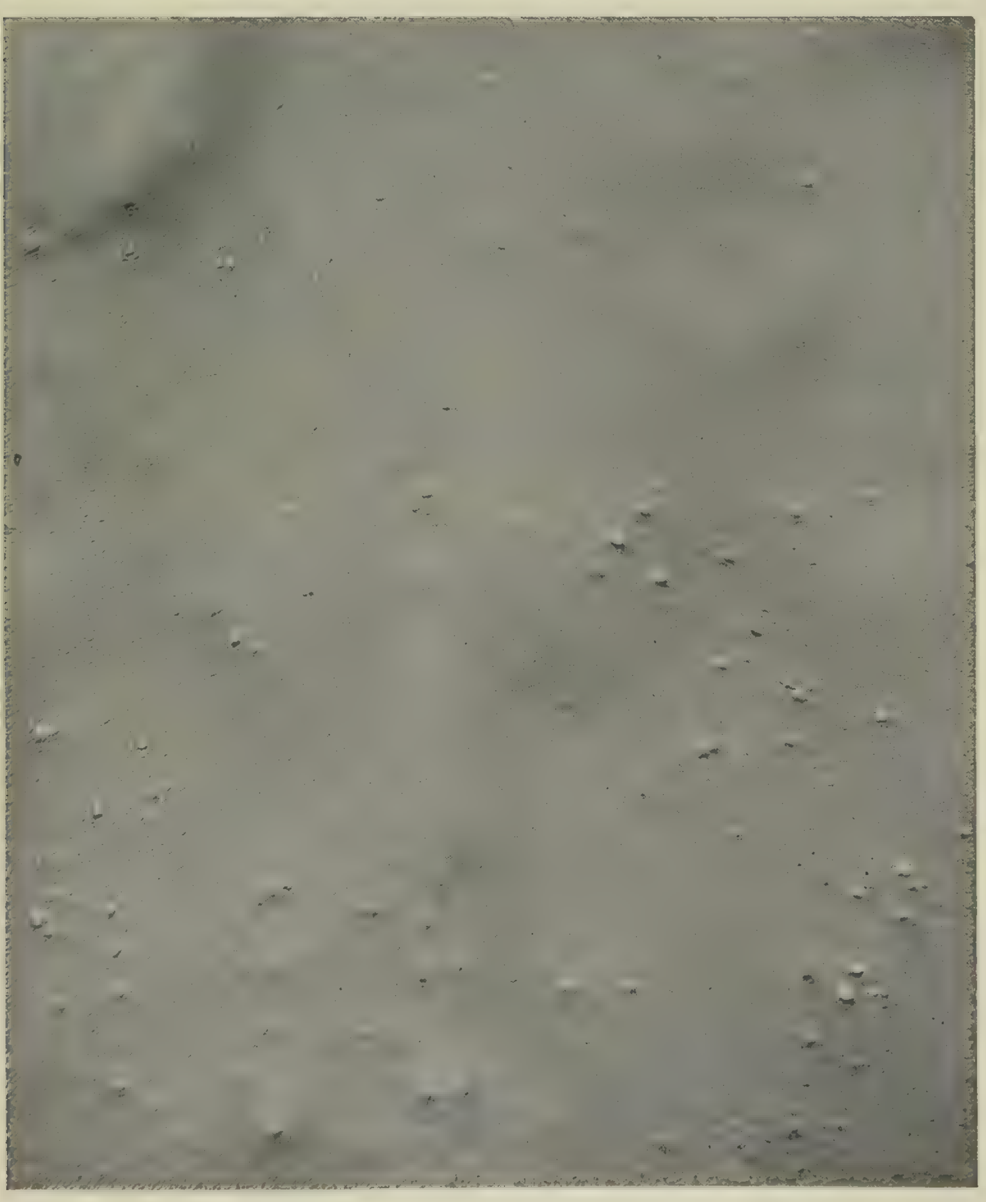


Fig. 178.—Small Acuminated Papulo-pustular Syphilide.

Pustular syphilides closely simulate non-specific lesions of the same nature. They are prone to form somewhat deep ulcers and on healing leave pigmented scars. They appear late in the secondary period, are often found associated with other syphilides, are obstinate to treatment, and readily recur. Their seats of predilection are the scalp, face, and legs, though they may appear on any part of the body. Their early development as a general eruption accompanied by fever, with pronounced impairment in general health, usually denotes a severe form of infection.

The small acuminated pustular syphilide (Fig. 178) is distinctly superficial and is an early lesion. The small pustules are placed about hair-follicles on ducts of sebaceous glands and form thin, yellowish crusts which may become confluent and resemble impetigo. The large acuminated pustular syphilide closely resembles acne; the pustules are slow to rupture.

The flat pustular syphilides, according to the size of the individual lesions, may resemble either impetigo or ecthyma, since both exhibit a tendency toward crusting. Syphilitic impetigo is, however, persistent, healing slowly and leaving permanent scars. Moreover, it is often confluent, forming irregular patches which exhibit circinate crusted borders surrounding an area of scarred and pigmented or sometimes nearly normal skin. This eruption is particularly prone to develop on the hairy portions of the face, about the nostrils and lips, and on the chest and the outer surfaces of the arms and legs. The confluent eruption is extremely resistant to treatment and usually occurs late in the disease.

The large flat pustular syphilide in its more superficial form occurs about the end of the first year and readily yields to treatment. On raising the crust there is found an erosion rather than distinct ulceration. The deep form is characterized by thick, stratified, black crusts covering a destructive ulceration about which there is an area of distinct infiltration. These lesions are termed rupial, are circular in shape, are usually discrete and, as a rule, comparatively few in number. They may run together, forming irregular patches of ulceration with circinate borders. These pustulo-crustaceous lesions, confluent and deep, form what are called the serpiginous ulcers. The syphilitic nature of the affection may be determined by the slow evolution of the lesion, its persistence, the absence of acute inflammatory symptoms, the depth of the ulceration, and the coincidence of other signs of syphilis. The affection yields slowly to constitutional treatment.

Vesicular Syphilides.—These rare eruptions may simulate eczema, varicella, or herpes, and may be general or grouped. The discrete vesicles are surrounded by a raw ham-colored areola which is characteristic. When confluent these vesicles may present the typical appearance of vesicular eczema, but will differ from the latter in that there is neither itching nor pronounced inflammation. Moreover, there are usually associated lesions of a papular or pustular nature and the internal administration of mercury is curative.

The varicelloid form may simulate closely varicella, except that the vesicles have their characteristic areola and the outbreak is unattended by fever.

These vesicular syphilides are prone to become pustular, and when constitutional symptoms are present from other causes the disease may readily be mistaken for varioloid. A history of the case and a period of observation and treatment may be necessary before a diagnosis can be formulated.

Pigmentary Syphilides.—The pigmentary syphilide must be distinguished from the discolorations which follow the ordinary secondary and tertiary eruptions of the disease. It occurs, as a rule, in the first year of syphilis and in young women, the seat of predilection being the sides of the neck. It appears in the form of rounded or irregular brown patches, sometimes showing leukodermatous changes, sometimes presenting the appearance of a marbling, lasts for some months, and is apparently

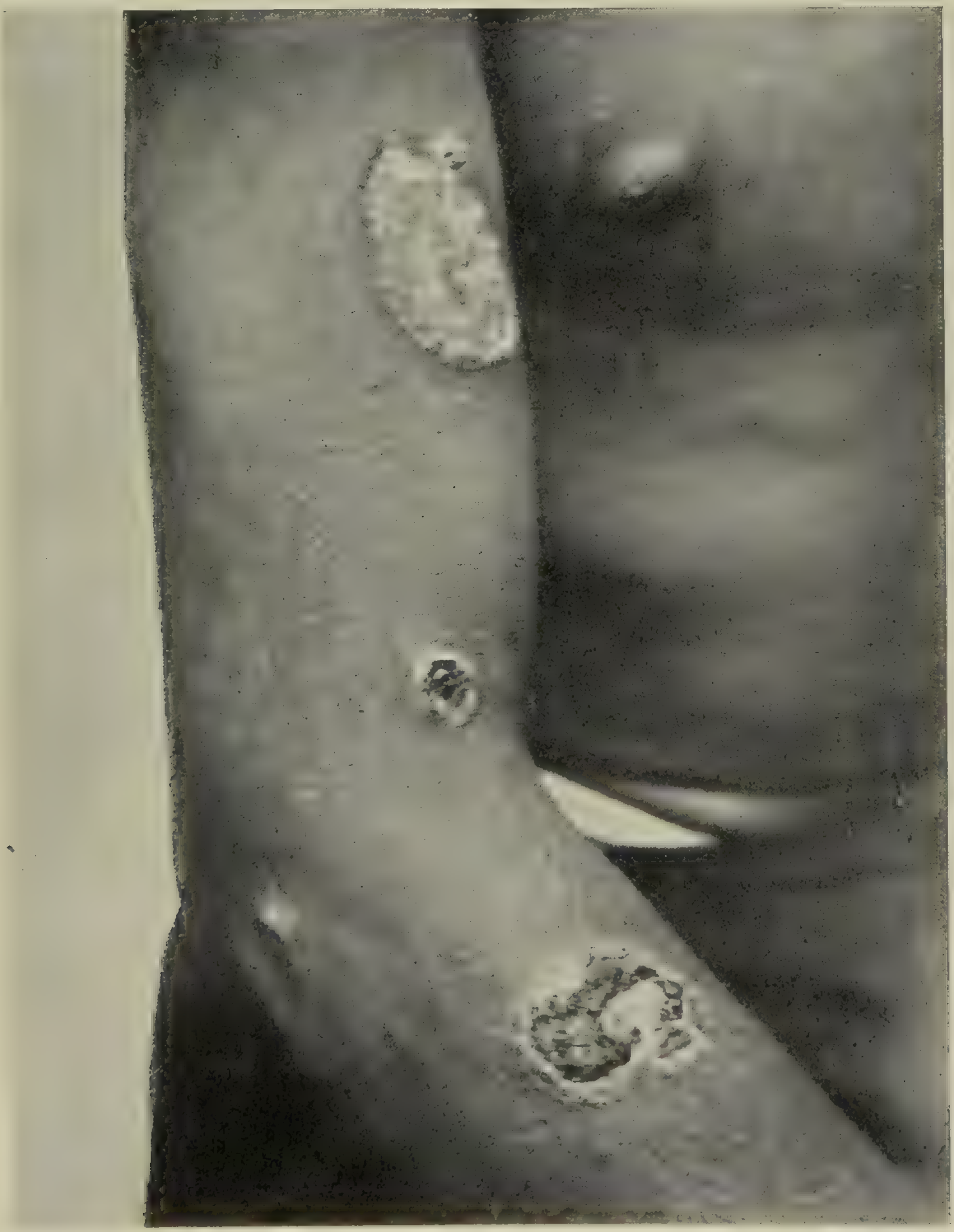


FIG. 179.—TUBERCULAR SYPHILIDE.

unaffected by the treatment, since it is in reality a parasyphilitic phenomenon.

Tubercular Syphilides.—These are, as the name implies, infiltrations of the entire thickness of the skin, presenting in the formative stage almost exactly the appearance of a beginning boil, except for the absence of the acute inflammatory phenomena which accompany the latter. The eruption is commonly grouped, the individual lesions exhibiting a tendency to coalesce (Fig. 179).

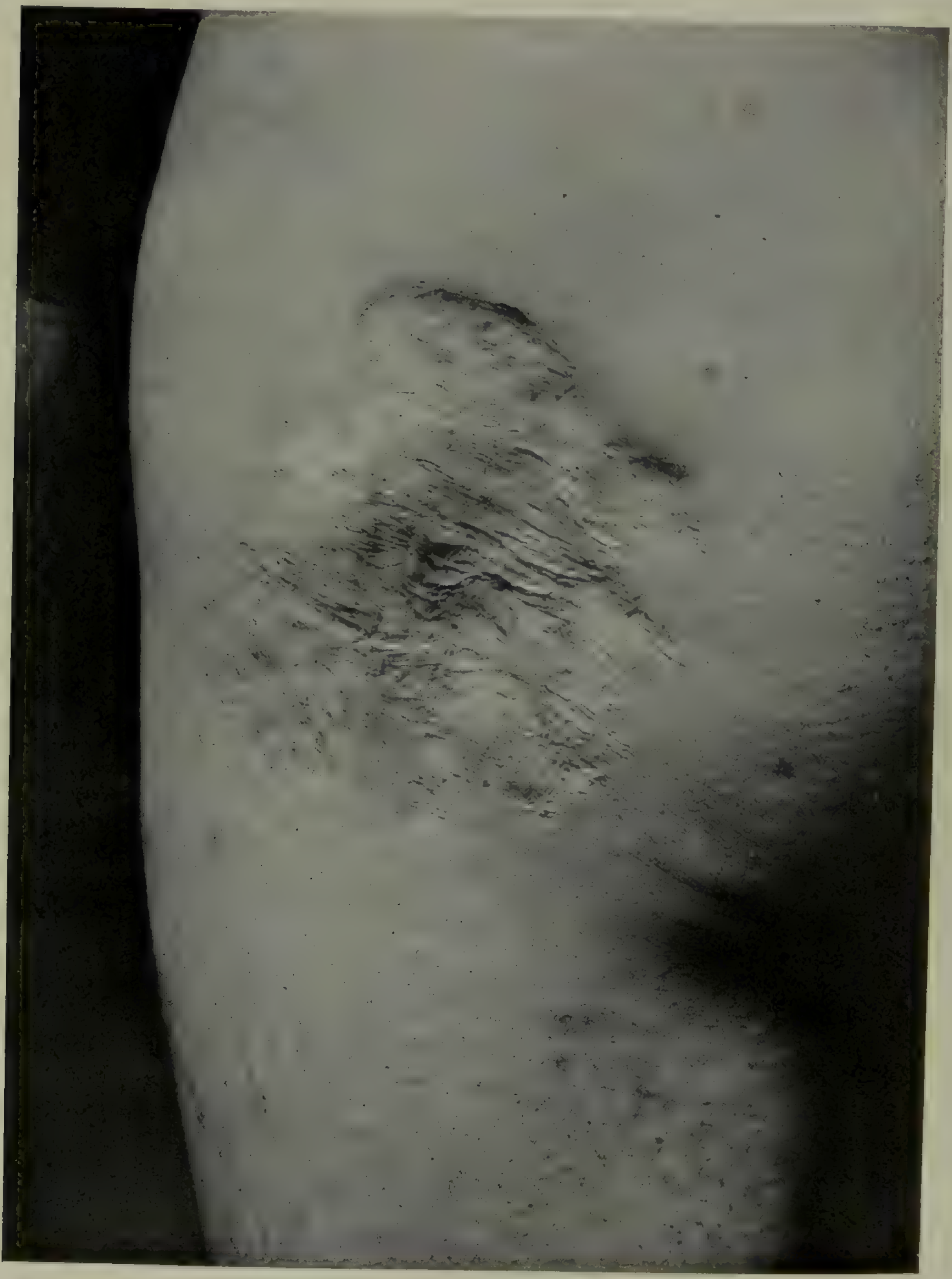


Fig. 180.—Typical Cicatrix of Tubercular Syphilide.

The seats of preference are the face, ears, back, and legs. On the face it is common about the nose, forehead, lips, and ears. The eruption may become absorbed or may ulcerate, in either case leaving permanent scarring.

It may remain discrete or become confluent. It is extremely persistent, is prone to relapses, and may occur at any period of the disease, though it is commonly a late tertiary. Tubercular syphilides are sometimes complicated by papillary hypertrophy, forming one or more cauliflower growths. The cicatrices of the ulcerating tubercular syphilides are highly characteristic, exhibiting in a large cicatrix the small round scars of the individual tubercles (Fig, 180).

The tubercular syphilide, particularly as it occurs upon the face, must be distinguished from lupus vulgaris. The latter affection commonly appears before the twentieth year of life, and in those without a syphilitic history it is extremely slow to break down, is attended by very slight skin infiltration, by superficial ulceration without regular form, and is unaffected by specific treatment, nor do the cicatrices exhibit the coppery stains and the circular scars of the tubercular syphilides.

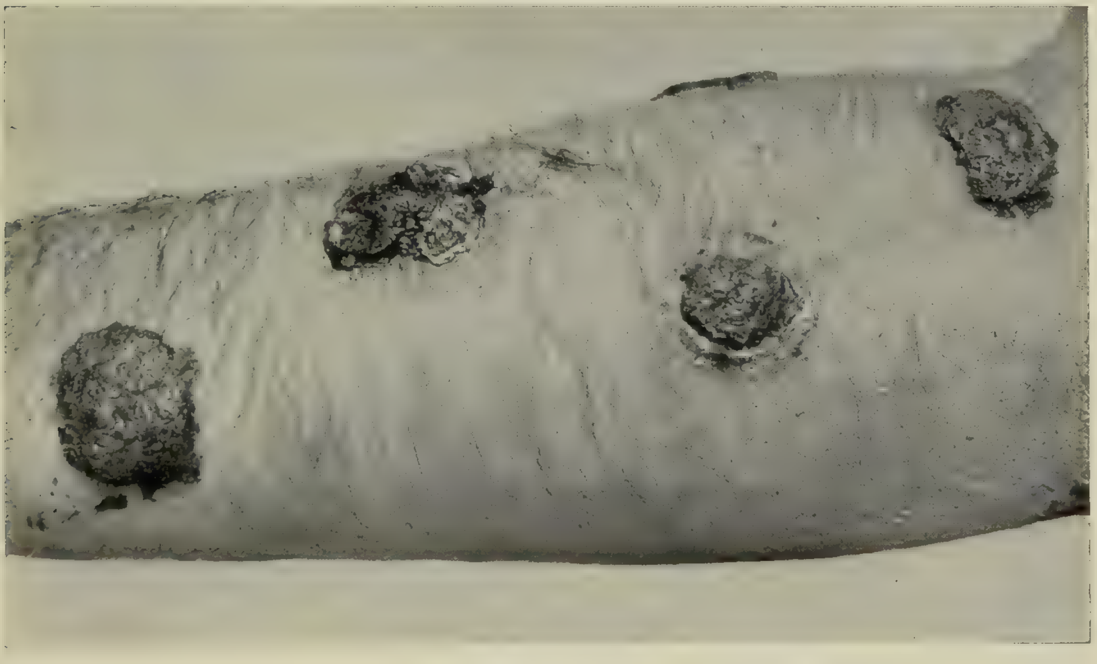


FIG. 181.—RUPIAL LESIONS, FOLLOWING BULLOUS SYPHILIDE.

Bullous Syphilides.—These appear as blebs of clear serum which shortly become pus, forming after rupture thick black scabs (Fig. 181), beneath which lie round, punched-out, deep, unhealthy ulcers. This late lesion of syphilis is highly characteristic not only of the disease itself but either of an inveterate form of it or of low tissue resistance.

Gummatous Syphilides.—These are characterized by the painless formation of tumors involving the skin and subcutaneous fascia, varying in size from that of a pea to that of a cherry, becoming slightly inflammatory in type, softening, breaking down, and forming deep sloughing ulcers. These lesions are expressions of the late period of the disease; when they occur early, they are characteristic of malignant syphilis. The gumma may be single or multiple; in the latter case it is likely to be grouped and made up of comparatively few units.

The favorite seats of the gummatous syphilide are the forehead, the upper third of the anterior surface of the leg, the arms and forearms, the skin over the clavicle and sternum, the scrotum, the penis, the back of the neck (Fig. 182), and the external genitalia in women.

Drunkards and those suffering from visceral disorders are subject to a diffuse infiltration of the face, producing the appearance of leontiasis. This readily breaks down under mixed infection, resulting in extensive ulceration and disfiguring scarring.

Gummata of the leg are commonly multiple, involving its upper third or the malleolar regions. Cutaneous gummata, when placed over bones superficially located, very commonly involve the latter. This is particularly true of the lesions overlying the frontal and nasal bones, the sternum, clavicle, and tibia.

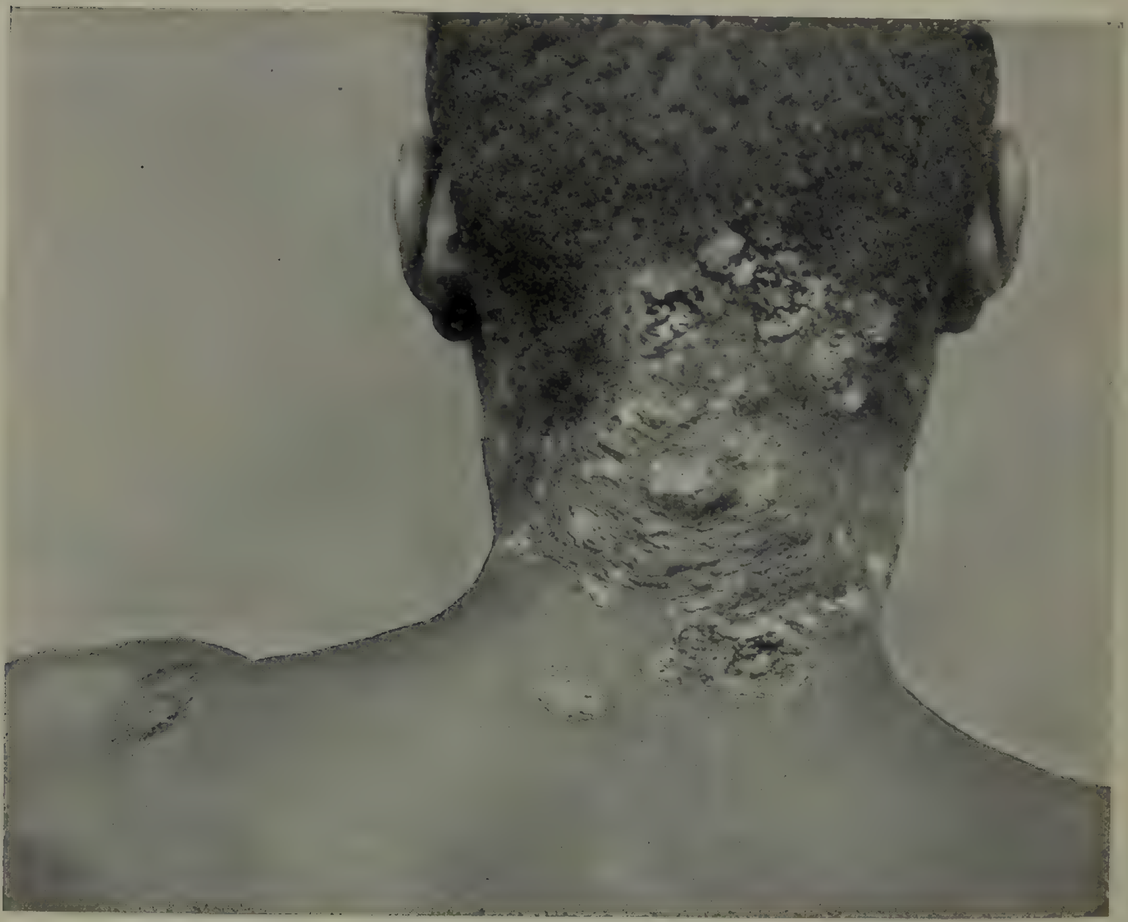


FIG. 182.—GUMMATOUS SYPHILIDE.

When the gummata become confluent and break down, huge serpiginous ulcers are formed, the underlying and surrounding tissues being steadily eroded by a progressive inflammation extremely resistant even to specific treatment. Sometimes these serpiginous ulcers exhibit fungous granulations closely simulating malignant growths. Since the gummata involve the subcutaneous tissue, the resulting cicatrices are adherent to the deeper structures.

As to the diagnosis of gummata, it may be said that any causeless ulcer developing in the regions of predilection, and persisting in spite of appropriate topical treatment, is probably syphilitic. Gummata of the prepuce or the glans penis during the ulcerative stage may exactly simulate chancre. A history of previous infiltration and the absence of inguinal gland enlargement and the secondary lesions following chancre may clear the diagnosis. The distinction between gumma and cancer is at times possible only by excision and microscopic examination of a portion of the infiltrate.

Syphilitic Alopecia.—Falling of the hair is an early secondary symptom and appears with the ordinary cutaneous manifestations of the disease. Usually there is a patchy alopecia, giving the scalp a moth-eaten appearance. At times there is a general thinning of the hair, most noticeable at the back of the head. Exceptionally there is a total loss of the hair. Recovery from the alopecia of early syphilis is usually complete. That caused by deep ulcerating lesions of late syphilis and circumscribed to the seat of these lesions is permanent.

Onychia.—The nutrition of the nail is sometimes profoundly affected by early syphilis, one or all of these appendages exhibiting a dry, lusterless, often deformed and discolored growth, or being completely loosened. These lesions are not attended by inflammatory phenomena, and are annoying only because of the unsightly appearance. They are followed by a new nail growth which may be entirely normal.

Paronychia, or inflammation about the roots of the nails, may be dry or ulcerating. In the former case it forms a painless infiltrate exhibiting a coppery color. In the latter case there is persistent ulceration, sometimes attended by exuberant granulations, and exceptionally accompanied by a swelling of the entire terminal phalanx. As a result of this ulceration the nail may be permanently shed, nor, if the matrix has been destroyed, will it be reproduced. When it does grow again, it is usually permanently deformed.

Lesions of the Mucous Membrane.—These correspond in general with those observed upon the skin, differing only from the fact that the mucous surfaces are more vascular, are kept constantly moist, and as a rule are more subject to irritation.

The erythematous syphilide may and probably does attack all mucous surfaces, becoming rapidly confluent. The syphilitic sore throat which commonly attends the first eruption of the constitutional disease is the commonest manifestation of the mucous erythema. On examination the half arches, the soft palate, the tonsils, and the pharynx may exhibit an acute hyperemia and edema simulating an ordinary sore throat. A similar condition may develop on the inner surface of the foreskin or on the glans penis, suggesting an ordinary balanoposthitis, or like lesions in the urethra or vagina may suggest simple infection of either of these mucous tracts. The discharges from any of these inflamed mucous surfaces are extremely contagious and it is important that their true nature be recognized.

The papular syphilides of the mucous membranes may appear as papular erosions or diphtheroid or vegetative papules. All these manifestations of syphilis are termed mucous patches.

Papular erosion, which is particularly common in those who abuse alcohol and tobacco, appears in the form of small or large, rounded, infiltrated, raw-ham colored, smooth patches, exhibiting a shining surface because denuded of epithelial covering. These are found mostly on the dorsum of the tongue and are associated with the diphtheroid papule.

The diphtheroid papule is characterized by a pseudo-membranous deposit covering a raw and readily bleeding surface. At times these patches exhibit ring-like configuration; at times they are attended by a papillary overgrowth producing a lesion called the vegetating papule, exhibiting the appearance of an infiltrated papilloma. Several of these lesions may become confluent.

The diphtheroid papule or mucous patch is one of the commonest and most frequently recurring lesions of syphilis. It is placed on the inner surface of the cheeks and lips, on the gums, on the soft palate, tongue, and at the angles of the mouth, where it is prone to fissure. In the latter case it may become painful; when placed on the tonsils it may form deep and crippling ulcers.

These lesions, being subject to mixed infection, give rise to inflammatory enlargements of the associated lymphatic glands.

Papulosquamous syphilides or scaly patches produce irregularly shaped, flat, almost translucent, bluish-white splashes, such as would be caused by painting the mucous membrane with a strong solution of silver nitrate. These may extend peripherally and heal centrally, and may coalesce, producing geographic markings. They are commonly observed on the buccal surfaces of the cheeks in smokers and on the inner surfaces of the lips. They occur late in the disease and are, as a rule, uninfluenced by constitutional treatment, constituting a parasyphilitic phenomenon.

SYPHILIS OF THE ALIMENTARY TRACT.

Upon the mucous membrane of the mouth the primary lesion occasionally develops; secondary lesions almost invariably. The gummatous infiltrations are more common in men than in women.

Upon the tongues of men gummatous lesions may be superficial or deep. The superficial gummata before ulcerating may reach the size of a cherry. By confluence they may destroy the greater part of the organ, or if attacked by acute inflammation may be accompanied by edema so rapid and pronounced as to threaten life.

The deep gummata involving the muscular substance of the tongue may reach the size of an egg, growing slowly for several months before softening takes place and resulting in disfiguring and crippling cicatrices. Diffuse gummatous infiltration produces an asymmetric induration and tumefaction, accompanied by a crippling of motion and followed by slow absorption and cicatricial contractures. The tongue in these cases appears enlarged and irregularly lobulated, with the overlying mucous membrane profoundly altered, areas of exfoliation alternating with fissured and eroded patches of thickened epithelium, presenting the appearance of lingual psoriasis.

The diagnosis of the early lesions of the mucous membrane of the mouth is formulated in the main upon their extent and persistence, together with the presence of other signs of syphilis. A mucous patch, if small, may present precisely the appearance of a herpetic lesion.

The late papulosquamous eruptions are so like the lesions incident to chronic inflammation that the diagnosis from the appearance of the spots can scarcely be formulated. It has also been clearly shown that many of these late lesions, though prone to appear on syphilitics, are parasyphilitic in nature.

The gummatous lesions can scarcely be confounded with any condition other than tuberculosis and malignant disease. The gumma customarily begins as an infiltrate of the dorsal surface of the tongue which slowly ulcerates, shows no local or general reaction to tuberculin injection, and is cured by the administration of mercury. None the less it happens at times that the diagnosis between malignant and syphilitic infiltration can be made only by microscopic examination of an excised portion of the growth.

Exceptionally as a symptom of tertiary syphilis there is noted pyorrhea due to specific infiltration of the bone. This in its symptomatology closely resembles the stomatitis due to mercury, but is cured by the administration of this drug.

The hard palate is subject to gummatous infiltration, in the form of one or more tumors in the middle line or near it. These slowly soften, exposing necrosed bone, resulting in an opening into the nasal cavity. When the infiltration begins on the nasal side of the palate bone, the presence of a swelling in the roof of the mouth denotes that the bone already has been destroyed. When the gummata are confluent they may destroy a considerable area of the palate, leaving permanent openings which can be closed only by extensive plastic operations.

Gummata of the soft palate commonly develop on the pharyngeal wall of this organ, exhibiting no symptom on inspection other than a slight swelling and edema, but manifesting their presence by a stiffness and immobility of this organ which is highly characteristic. Whether the infiltrate be circumscribed or diffuse it is prone to rapid ulceration and destruction, resulting in cicatricial deformity. Adhesion of the soft palate to the posterior pharyngeal wall, its loss of suppleness, or its complete absence, are common sequels. A gummatous ulceration beginning at the triangle formed by the junction of the anterior and posterior arches and the upper surface of the tonsils may involve all these structures in extensive destruction.

The pharynx may present the manifestations of early syphilis, particularly the mucous patch in the typical form; the gummatous lesions are, however, more common and are likely to be persistent and painful, resulting in cicatrices and adhesions to the half arches and palate. The ultimate result may be impairment in phonation and an inveterate form of nasopharyngeal catarrh.

Gummatous infiltration may attack any portion of the gastro-intestinal tract. The comparatively few cases found at autopsy or detected clinically seem to show that this involvement is rare; there are, however, undoubted instances of stricture of the esophagus due to the healing of gummatous infiltrates. Moreover, there are instances of gastric ulcer apparently cured by specific treatment. If the small intestine is involved in syphilitic ulceration it will be in its upper portion.

Gummatous infiltration of the rectum is a well recognized manifestation of late syphilis. It commonly begins just within the internal sphincter, appearing in the form of multiple nodules which, either by ulceration or interstitial absorption, finally form intractable strictures. At times these coalescing ulcers exhibit exuberant granulations closely simulating the appearance of malignant growth. Perirectal gummata reach comparatively large size before rupture into the gut and prepare the way for the formation of ischiorectal abscesses and fistulæ which are likely to be multiple and persistent. The symptoms of gummatous infiltration of the rectum are at first those of a proctitis characterized by a morning diarrhea, accompanied by pus and blood; later, when the ulcer extends within the grip of the sphincter, there may be pronounced pain during and after defecation; when stricture develops defecation becomes more difficult and the movements are not formed.

The prognosis of the well-advanced cases of specific proctitis, whether they be infiltrating or ulcerating, must be guarded, since specific treatment is without avail when the disease reaches the stage of scar formation. During the infiltrating and ulcerating stage appropriate general and local treatment is likely to accomplish a cure. In the early cicatricial stage repeated dilatation is serviceable. In the late cicatricial stage excision of the rectum is indicated.

SYPHILIS OF THE RESPIRATORY TRACT.

Primary syphilitic lesions are exceptionally observed in and about the nares. The secondaries appear in the form of moist papules. Gummata are comparatively common, particularly in the hereditary form of the disease, and, involving bone and cartilage, may produce rapid, extensive, and disfiguring permanent lesions.

Acute rhinitis, extremely common in hereditary syphilis, is rare in the acquired form of the disease. It is characterized by its persistence and by the formation of erosions and ulcers. It may run into the hypertrophic and ultimately the atrophic form. The diagnosis depends entirely upon the history, the presence of other characteristic lesions, and the effect of specific treatment.

The gummata may be nodular or infiltrating in type; they attack by preference the cartilaginous septum and the floors of the nasal canals. They cause erosion of underlying cartilage or bone, resulting in openings into the mouth, through the septum, or upon the overlying skin. The infiltrating form is prone to slough and is accompanied by widespread necrosis. These breaking-down infiltrates are characterized by persistence, foul odor, and detection of dead bone on examination. Such lesions are usually late tertiaries, though they may be premature. The treatment consists in thorough cleanliness, constitutional medication, and removal of dead bone.

The larynx in the early constitutional stage may show a simple acute erythema or may exhibit mucous patches which become converted into erosions, or exceptionally into true ulcers. The late lesions appear in the form of diffuse gummatous infiltration or circumscribed gummata.

Because of the absence of pain alteration of the voice is usually the first symptom. True gummata form first rounded tumors, particularly on the epiglottis, aryepiglottic folds, the vocal chords and posterior walls of the larynx, or these may be converted into deep and destructive ulcers, resulting in cicatrization and interference with function. In the early stage of gummata acute edema may develop so rapidly as to cause death from suffocation.

Syphilitic lesions in their ulcerating form may simulate either tuberculosis or cancer. In the main the diagnosis will be based on the history of the case associated with the presence of other specific manifestations, the absence of tuberculous lesions elsewhere, negative tuberculin test, and microscopic examinations of portions of the diseased tissue.

There have been some cases of gummatous infiltration of the trachea and bronchi reported followed by softening and breaking into surrounding organs or by cicatricial contracture. The symptoms are mainly persistent harassing cough, bloody expectoration, and pain and tenderness behind the sternum.

The lungs may be affected in the early stages of syphilis, in the form of acute congestion. Usually in the late stage the disease manifests itself either in the form of diffuse sclerosis or circumscribed gummata; at times in the apices, but usually in the middle third. The symptoms of either diffuse or circumscribed infiltrates are precisely those of pulmonary tuberculosis. The progress is slow, a cavity forms usually in the mid-portion of the lung, hectic develops. The diagnosis is based on a syphilitic history with the finding of associated symptoms, absence of the tubercle bacilli, and the results of constitutional treatment.

SYPHILIS OF THE BONES AND JOINTS.

Syphilis exhibits a special predilection for the osseous system. The lesions may be precocious, developing before the cutaneous eruption or shortly after it; as a rule, they occur in the late period of the disease. The lesions are prone to occur at the seats of former traumata; it therefore happens that bones most superficially placed are commonly involved.

Precocious lesions in the form of osteoperiostitis appear as circumscribed bone swellings, usually extremely painful and tender. They are commonly found on the frontal and parietal bones and the anterior surfaces of the tibias. They may disappear completely or leave permanent thickening. The late lesions, appearing in the form of osteoperiostitis, osteitis, or osteomyelitis, are sometimes without subjective symptoms, though they also may be characterized by harassing pain. They are both pathologically and clinically similar to granulomatous bone lesions due to other causes, differing only from the fact that they are cured by specific treatment.

Gummatous osteitis and osteomyelitis may be circumscribed or diffuse and may involve any bone of the body, either peripherally or in its central portion. It may be complicated by caries and necrosis, resulting in a worm-eaten appearance of the bone. There is, as a rule, a peripheral formative osteitis. Absorption may take place in the absence of suppuration. In the flat bones the lesions often exhibit a circinate grouping.

Gummata of the cranial bones may cause multiple perforation of the skull (Fig. 184). The rounded ulcers which develop as a consequence of ulceration give a scanty discharge. The examining probe at once touches dead bone.

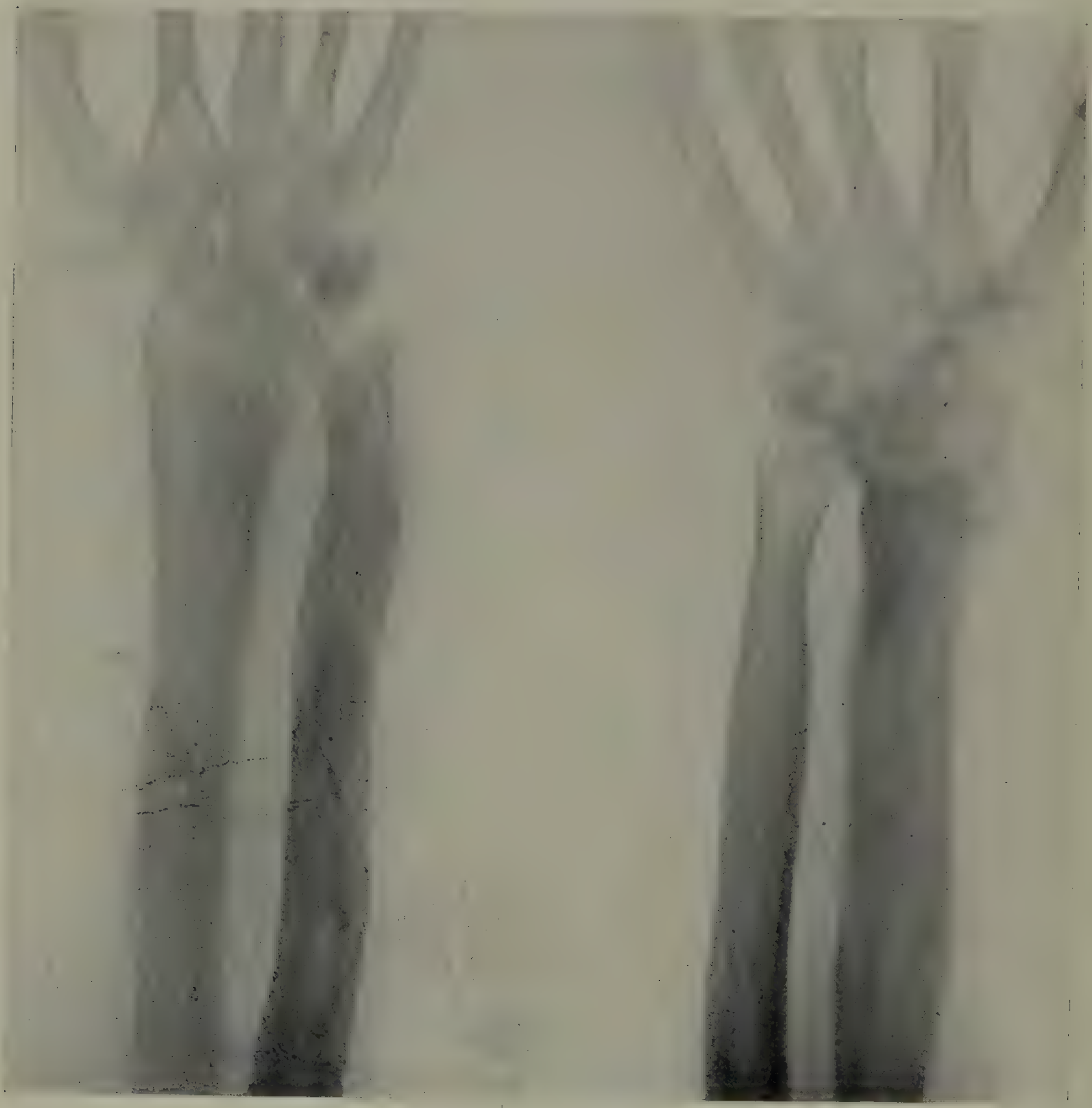


FIG. 183.—SYPHILITIC OSTEOMYELITIS.

The development of gummata in the vertebræ may closely simulate Pott's disease, the same symptoms and sequels appearing.

Of all the long bones, the tibia is the one most commonly involved.

Syphilitic dactylitis is a common manifestation of hereditary syphilis. In the superficial form the soft parts about the joint are involved. The deep form attacks the entire tarsus, including the bone and periosteum, though it may be limited to the opposed surfaces of two phalanges. Usually several fingers or toes exhibit the lesions, fusiform swellings forming, into which, as a result of ulceration, sinuses pass, communicating in the deep form with dead bone. In the absence of ulceration there is likely to be absorption. The ultimate result is a deformed, flail-like, or ankylosed joint.

Syphilitic involvement of the joints in the early period of constitutional disease is often characterized by severe pain. This may precede the first eruption and may be so severe as to constitute a true arthralgia. Exceptionally there develops synovial effusion into one or many joints. This is characterized by both the local and general symptoms of acute articular rheumatism. When only a single joint is affected the knee is usually the one of choice.

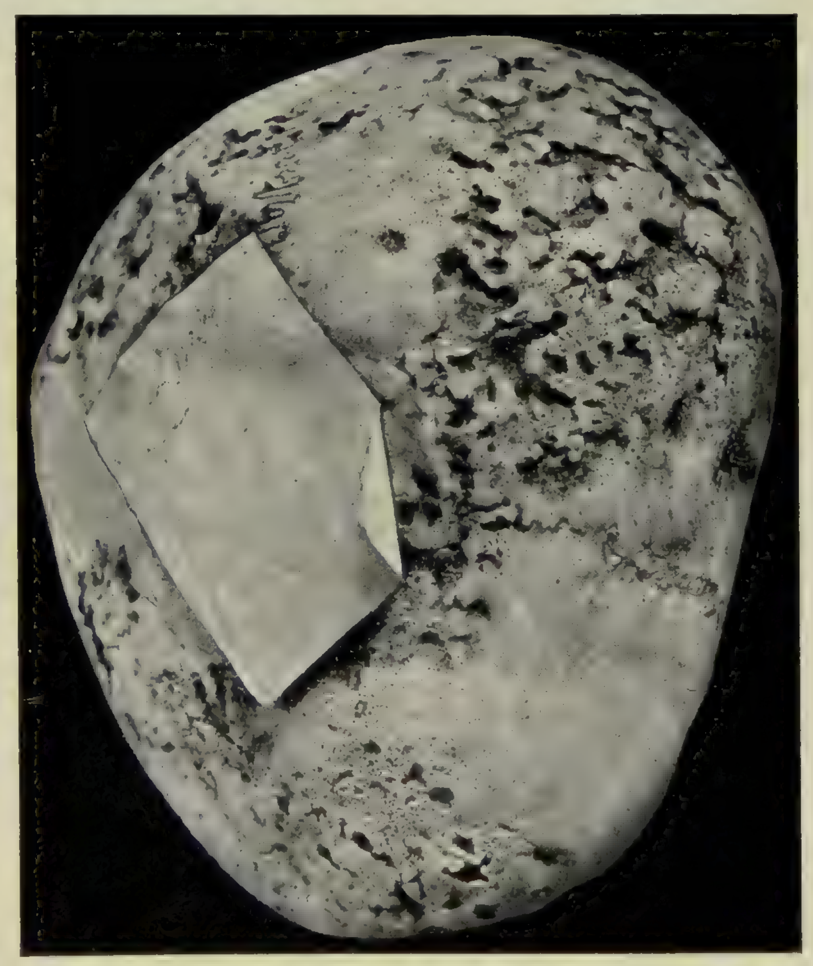


FIG. 184.—SYPHILITIC OSTEOMYELITIS.

Synovitis in the late stage of the disease is more likely to assume the form of hydrarthrosis.

Gummatous arthrosis, a late manifestation of syphilis, is characterized by infiltration primarily of the ligaments and secondarily of the synovial membranes and the articular cartilages. The knee, the sternoclavicular joint, the wrist, and the ankle are the joints commonly involved. The affection develops first as a tumor, not sharply circumscribed but involving part or the whole of the joint. The subjective symptoms are often extremely mild, but at times (and this is particularly the case when the gummatous involvement is primarily in the bone) the pain is excruciating, being particularly distressing at night.

In its symptomatology the affection closely resembles tuberculous involvement. Both may lead to total destruction of the joint, and a distinction can be made only by a careful consideration of the history and by the use of the tuberculin and therapeutic tests. Exceptionally gummatous arthrosis develops an as acute affection, in which case it resembles rheumatism. The tuberculous joint lesion is more prone to ulcerate and discharge externally than is the gummatous, though the latter may exhibit the same phenomena.

Early treatment in these cases brings about resolution. Later changes due to atrophy or suppuration are irremediable and are to be treated on ordinary surgical principles supplemented by the internal administration of mercury and potassium iodid.

Acute bursitis of syphilitic origin is extremely rare. Gummatous bursitis is somewhat more common and usually involves the prepatellar bursa, forming a nodular fluctuating swelling which is prone to ulcerate.

SYPHILIS OF THE MUSCLES.

Acute syphilitic myositis exceptionally develops in the early stages of the constitutional disease and is characterized by pain aggravated by pressure or motion. It is especially likely to attack the humeral biceps, holding the muscle in a condition of tonic contraction, thus seriously interfering with function.

In its late manifestation syphilis may attack muscles in the form of a chronic myositis or gummata. The former attacks the muscular fiber, resulting in contractures and atrophy. It involves the sphincter of the anus and the biceps. The symptoms are characterized by pain, tenderness, and diffuse muscular swelling followed by wasting and shortening. The affection is often mistaken for rheumatism. It is, however, apparently causeless, slow, persistently progressive, and yields to constitutional treatment.

Gummata form circumscribed tumors which are prone to soften and discharge. They are usually painless unless the growth be extremely rapid, and rarely reach a size larger than a man's fist, though exceptionally they are four times as large. They are most frequently found in the trapezius, pectoralis major, biceps, and lingual muscles. They simulate most closely tuberculosis and malignant infiltrations, and can be distinguished from the latter only by the therapeutic test.

Tenosynovitis may assume an acute form in the early stages of syphilis. It is characterized by crackling and superficial pain and tenderness; exceptionally it develops in a chronic form, in which case there is neither pain nor tenderness but a thickening and possibly a limitation of motion. In the gummatous form of the disease tumors are formed along the course of the tendons, particularly the tendo Achillis and biceps.

SYPHILIS OF THE BLOOD-VESSELS.

Syphilitic involvement of the heart occurs late in the course of the disease, in the form of diffuse, chronic myocarditis or gummata. In the former case there are disseminated patches which ultimately become converted into cicatrices. They are commonly found in the wall of the left ventricle.

Gummata may reach the size of a pigeon's egg. The symptoms are those of a myocarditis. Death is likely to be sudden.

Syphilitic arteritis may begin peripherally, finally involving all the coats of the vessel, not only destroying its elasticity but narrowing or even obliterating its lumen. Endarteritis usually appears in the sclerous form, the infiltrate becoming converted into opaque patches of hardened fibrous tissue which may be disseminated or may involve the entire circumference of the vessel. It is a common cause of aneurism.

The vessels of the brain are those particularly attacked, especially the end-arteries, producing degeneration of nerve cells and profound psychic and motor central changes.

The prognosis in these cases is bad, as the condition is rarely suspected until irremediable damage to the brain cells has been produced. In aneurism and angina symptoms of endarteritis are at times relieved or cured by treatment.

Phlebitis is a rare expression of syphilis. It is accompanied by thrombosis, which is superficial and multiple and yields to specific treatment.

SYPHILIS OF THE LIVER.

The very early stage of constitutional syphilis is exceptionally accompanied by a symptomless and painless hypertrophy of this organ which promptly disappears under specific treatment. Calvert has collected over 100 cases of early syphilitic jaundice characterized by the rapidity of its appearance, its tendency to recur, its disassociation from digestive disturbances, and its rapid disappearance under treatment.

The late manifestations of hepatic syphilis may take the form of diffuse gummatous infiltration or the development of circumscribed gummata. The former appears usually in disseminated patches, is accompanied by perihepatitis and adhesions to surrounding organs, and is ultimately converted into connective tissue which by its contraction narrows or obliterates the hepatic ducts, causing atrophy of the liver cells.

During the period of infiltration and hyperemia the liver is enlarged. Later it becomes smaller than normal, presenting a lobulated and distorted appearance.

Gummata are commonest about the region of the suspensory ligament and along the course of the portal vein, and may be grouped or disseminated. They undergo central degeneration and absorption, the peripheral portions becoming converted into fibrous tissue, producing great distortion of the organ. There is commonly an associated perihepatitis, causing lesions of the surrounding structures; this is particularly marked on the upper surface of the liver.

Amyloid degeneration is often associated with both forms of hepatitis.

The symptoms of the syphilitic hepatoses are vague, the diagnosis being based first on the hypertrophied, afterward on the atrophied and distorted nodular liver. Jaundice is exceptional, but hematemesis, digestive disturbances, edema, and ascites are common, as in other forms of cirrhosis. A distinction from cancer is at times most difficult. At times this ascites develops without premonitory symptoms.

The prognosis of the disease in its advanced form is bad.

SYPHILIS OF THE SPLEEN.

The spleen is usually involved in the early stages of syphilis in the form of a painless, symptomless enlargement which subsides in the course of weeks or months. In the later stage of the disease there may be gummatous infiltration, attended by such inconspicuous symptoms that it is not detected during life. Marked leukocytosis and the finding of pigmented placques in the blood are suggestive of gummatous splenitis.

SYPHILIS OF THE KIDNEYS.

The kidneys exhibit a tendency to precocious involvement characterized by a transitory, intermittent moderate albuminuria, perhaps accompanied by the presence of a few hyaline casts. This disappears under specific treatment and is often coincident with the first cutaneous outbreak. In the late stage of the disease the effect of the syphilitic toxins may be manifested as either parenchymatous or interstitial nephritis, each presenting precisely the symptoms of these conditions incident to other causes.

The diagnosis is based on examination of the urine, on the history of syphilis, and on associated signs of the disease.

Gummatous nephritis is rare and is usually associated with interstitial nephritis.

Amyloid degeneration, often associated with a similar condition of the spleen and liver, is a not uncommon manifestation of late syphilis.

The treatment is that appropriate to Bright's disease in its various forms, supplemented by the administration of mercury and potassium iodid, which must be given with extreme caution.

SYPHILIS OF THE EPIDIDYMIS AND TESTICLE.

Involvement of the epididymis alone in the syphilitic process is comparatively rare. Exceptionally the induration is acutely inflammatory in type, appearing in the form of circumscribed, rounded tumors in the head of the epididymis and involving the entire epididymis. Usually the attack is more chronic in type, appearing in the form of one or more nodules in the head of the organ, attended at most by very slight subjective symptoms. The gummata which develop in the late tertiary period are prone to soften and ulcerate.

The distinction must be made from gonorrheal epididymitis and tuberculosis. The former affection involves the tail of the epididymis and is secondary to urethritis. Moreover, it is more acutely inflammatory in type and is commonly accompanied by hydrocele. The tuberculous infiltration, which also, as a rule, involves the head of the epididymis, may so closely simulate syphiloma that the diagnosis can only be made on the basis of associated symptoms, tuberculin injection, the therapeutic test, and the finding of tubercle bacilli.

Orchitis is one of the commonest manifestations of syphilis. It may occur early in the disease or as a late manifestation, usually about the third year. The sclerous and gummatous forms are commonly associated, but one may predominate over the other. The affection is often bilateral and is unattended by subjective symptoms. The tumor formed is never larger than the fist. The cord is not enlarged and the outlines of the mass may be either smooth and symmetric or bossed and ridged. The growth is slow, requiring months for its evolution, and there is at times an accompanying and masking hydrocele. Exceptionally the disease begins as an acute orchitis, attended by pain, tenderness, and inflammatory symptoms. Gummatous orchitis may undergo interstitial absorption, followed by partial or complete atrophy, or may ulcerate, completely destroying the testis.

The diagnosis is based upon association with other syphilitic symptoms, the apparent causelesness of the infiltration, though rheumatism is a distinct predisposing factor, the absence of involvement of the cord and the epididymis, and the reaction to constitutional treatment. The distinction must be made from malignant and tuberculous disease. The former is rapid in its course and reaches enormous dimensions. The tuberculous orchitis begins, as a rule, in the epididymis, occurs before the age of thirty, and is customarily associated with thickening of the cord and involvement of the seminal vesicles, prostate, or other parts of the urogenital tract.

Even when the testicle is greatly enlarged by the syphilitic infiltration, a vigorous treatment may bring complete restitution to normal. After atrophic and cicatricial changes have set in the prognosis as to function must be more guarded.

SYPHILIS OF THE MAMMARY GLAND.

Syphilitic lesions of the breast, with the exception of chancre and manifestations in the skin, are extremely likely to be mistaken for malignant infiltrations. During the early constitutional period both men and women may exhibit an acute mastitis, characterized by pain, tenderness, and swelling. The gummatous mastitis occurring late in the disease may appear in the form of a dense infiltration of one or both breasts, followed by atrophy and contracture, or as one or more hard, circumscribed nodules.

The diagnosis from cancer may be quite impossible, except from a consideration of associated symptoms and the result of therapeutic treatment. The associated lymphatic glands are not enlarged.

SYPHILIS OF THE EYE.

The primary and secondary lesions of syphilis have been observed upon the eyelid and the conjunctiva.

As a late manifestation of the disease diffuse gummatous infiltration of the tarsal cartilages, usually chronic, producing great thickening and yielding only to mercury, is occasionally observed. Gummatous infiltration of the orbital walls behind the capsule of Tenon may result in optic neuritis and inflammation of the cornea. It is usually characterized by pain, restricted motion of the eyeball, and strabismus.

Syphilitic infiltration of the lacrymal gland is sometimes observed, forming a painless tumor, and prelacrymal abscesses are not uncommon manifestations of hereditary syphilis. The lacrymal sac and nasal duct are involved only secondarily by the gummatous infiltration of the surrounding bone, producing stenosis.

Interstitial keratitis is a common manifestation of hereditary syphilis, involving the entire thickening of the cornea, and producing a general haziness with marked vascularity. Ulceration is rare. Punctate keratitis appearing in the form of cloudy dots, triangularly arranged in the posterior layer of the cornea, is a late manifestation of syphilis, both in hereditary and acquired form, and is usually secondary to involvement of the deeper portions of the eye. Gummatous scleritis and episcleritis are sometimes observed.

The commonest affection is iritis, which may be plastic, parenchymatous, gummatous, or serous.

Plastic iritis is an early manifestation of the disease, characterized by discoloration of the iris, immobility of the pupil, injection about the cornea, abnormal reaction to mydriatics, posterior synechiæ, and severe pain, particularly marked at night.

Parenchymatous iritis occurring in the secondary stage of the disease is characterized by the formation of one to four minute nodules on the pupillary margin and is frequently complicated by synechiæ.

Gummatous iritis is a late manifestation of the disease characterized by the development of large nodules on the ciliary border of the iris.

Serous iritis, the rarest form, is accompanied by a punctate keratitis and hazy cornea, and is characterized by increased depth of the anterior chamber and slight dilatation of the pupil.

Both eyes are usually attacked in iritis.

The iritis of young children is practically always due to syphilis. The prognosis is good if treatment is instituted early. This consists in atropin, temporal venesection, the vigorous use of constitutional treatment, and in obstinate cases subconjunctival injections of bichlorid of mercury.

Choroiditis and retinitis develop, as a rule, in the first two years of syphilis. Opacities of the vitreous humor and atrophy of the optic nerve may result.

The usual cause of paralysis of the external muscles of the eye is syphilis, the lesion being commonly gumma at the base of the brain or in the orbit. The oculomotor is the nerve commonly affected, and this palsy may be the forerunner of tabes or general paralysis.

SYPHILIS OF THE EAR.

Aside from the ordinary eruptions of the early constitutional disease condylomata are the commonest lesions of the meatus.

Suppuration of the middle ear is commonly secondary to ulceration of the throat. Painless otorrhea is a usual symptom of hereditary syphilis. Labyrinthine involvement is a tertiary manifestation characterized by tinnitus, vertigo, and sudden, apparently causeless, deafness. The prognosis should be extremely guarded.

SYPHILIS OF THE NERVOUS SYSTEM.

With the exception of the headache accompanying, sometimes preceding, the first skin and mucous membrane outbreak of constitutional syphilis, lesions of the nervous system belong to the tertiary manifestations of the disease, commonly developing in the third or fourth year of infection, though they may appear in the first few months or may be postponed for many years.

Late cerebral manifestations of the constitutional disease are commonly observed in those of a nervous temperament, and are as prone to follow the mild as the severe type of the disease. The commonest predisposing factor is inadequate treatment of syphilis in its first two years.

Syphilis may attack the brain as a diffuse gummatous infiltration of the meninges involving the brain substance, gummata or circumscribed tumors may form, or endarteritis may develop with secondary brain lesions. The usual lesion found at autopsy is a low grade of proliferating meningitis. The dura mater most commonly exhibits this lesion, the resulting patches of chronic pachymeningitis resembling closely those produced by other causes. The arachnoid is rarely involved, but the pia mater very frequently shows sclerotic and gummatous changes which invade the encephalon, extending along the vessels as plates or bands, especially marked about the Sylvian fissure.

Syphilitic infiltrations are commonest on the frontal and sphenoidal surface of the brain. Gummata of the brain are always of comparatively slow growth. When they involve the dura they may reach the size of an egg, producing the pressure symptoms of any tumor.

Small obliterating nodules may form along the arteries. Syphilitic arteriosclerosis is probably the most important factor in the causation of specific cerebropathies. It may result in aneurismal dilatation and hemorrhage, ischemia incident to narrowing of the lumen of the vessels, thrombosis, or embolism. The brain and meninges may be involved secondarily by a syphilitic process attacking the bones of the skull.

The symptoms of cerebral syphilis are those incident to pressure, ischemia, and degeneration, and differ in no way from those incident to similar lesions from other causes. Syphilitic neuroses, however, are especially characterized by the multiplicity and incoördination of their symptoms. Moreover, if the prodromal headache be excepted, sensory disturbances do not form prominent features of the symptomatology.

The earliest symptom of cerebral degeneration, usually due to arteritis, is an apparently causeless development of neurasthenia.

This is often associated with a failure of memory, lassitude, restlessness, insomnia, headache, exhibiting a tendency toward exacerbation in the late afternoon and night, and a dread of impending misfortune. The symptoms of the further progression of syphilitic degenerations are those incident to interference with function from ischemia or pressure, and since, aside from the endarteritis, the commonest manifestation of syphilis of the brain is pachymeningitis, the pressure symptoms are most likely to appear in the form of palsies of the cranial nerves. Those also caused by gumma or involvement of the nerve-sheaths may follow the prodromal headache or may develop quite suddenly when the patient is in apparently perfect health.

Any of the cranial nerves may be involved, though the oculomotor is the one commonly affected. The sole symptom may be dilatation of the pupil. Usually there is external strabismus, ptosis, and paralysis of accommodation.

Neuritis and hyperesthesias are evidences of involvement of the fifth pair.

The sixth pair commonly escapes. When attacked, there will be diplopia and convergent strabismus, often associated with orbital neuralgia. Involvement of the seventh nerve occurs early, at times with the first manifestations of constitutional syphilis. It may appear simply in the form of paralysis of the muscles of the face, or, if the lesion lies deeper back, it may be associated with headache and tic.

The prodromal headache, especially when associated with an apparently causeless neurasthenia and loss of mental power, is of cardinal importance from the diagnostic standpoint, since if this period be passed without treatment irremediable injury results.

This prodromal headache is characterized by intensity and persistence, with daily exacerbations in the late afternoon or evening.

It must be distinguished from the parasyphilitic headache, which, though doubtless the result of the disease, is not a forerunner of paralysis and is not in the least influenced by treatment. It is harassing and persistent rather than crippling and daily recurrent, and corresponds to the type commonly observed in neurasthenia.

Neuralgic headache appearing in the form of neuritis, which is particularly prone to involve the supraorbital branch of the fifth pair, may be observed in both the secondary and tertiary stages of the disease. It can be distinguished from other forms of toxic neuritis only by the therapeutic test of vigorous treatment.

The severe cephalalgias attendant upon bone lesions are distinguished by their superficial localization and by their association with tenderness upon tapping or pressure.

Following the cephalalgia, neurasthenia, and general impairment of health by an interval of weeks or months, epileptiform or apoplectic attacks occur, often without complete loss of consciousness. These may be preceded by irregularly distributed paralysis of the cranial nerves, particularly of the oculomotor and abducens. In the absence of treatment the attacks of apoplexy are repeated, and finally merge into coma and death.

The characteristic feature of all the cerebropathies is their slow but persistent progression. Chorea, hydrocephalus, Ménière's disease, meningitis, myelitis, paraplegia, progressive paralysis, tabes, in fact, any or all of the cerebropathies may be so closely mimicked by syphilis as to make a distinction impossible, except by the therapeutic test.

In forming the diagnosis of the syphilitic nature of these affections a history of the disease is of prime importance. If, however, they develop without other adequate cause in a person of previously good health between the ages of twenty and forty-five, they are in all probability of syphilitic origin. It is true that any toxic condition such as gout will, by producing arteriosclerosis, cause similar symptoms. A distinction as to the nature of the affection must rest in the main upon the history of the case, the age of the person afflicted, and the therapeutic test.

Isolated palsies of cranial nerves, in the absence of other obvious causes such as traumatism, are nearly always syphilitic. Insomnia is customary in patients under fifty, somnolence in those over this age. Paralysis developing during sleep is customarily thrombotic in nature, and that coming on during periods of activity is more likely to be due to rupture. Epilepsy developing in an adult, if not traumatic or uremic or neoplastic, is syphilitic. Apoplexy occurring in men under fifty, free of renal or cardiac degeneration and not drunkards, is practically always syphilitic.

The prognosis in all these conditions is grave, though distinctly less so than that of similar conditions due to other causes. The success of treatment is in direct proportion to the promptness and vigor with which it is applied. When the endarteritis has reached the obliterating stage, treatment is quite futile.

Syphilis of the spinal cord is characterized by precisely the symptoms indicative of myelopathies from other causes. The lesion may appear in the form of diffuse infiltrations followed by sclerosis, or of gummata. They are common in the third and fourth years of syphilis, but may develop late and are predisposed to by venereal excesses during the active period of the disease and by exposure to cold. Fibroid degeneration and softening of the cord are often associated. At times this structure is secondarily involved by gummata of the bony envelopes, but this is much less common than is the case with the brain.

The commonest prodrome is loss of control over the bladder. This is often associated with loss of sexual power and partial incontinence of the anal sphincter.

Acute syphilitic meningomyelitis is characterized by vesical disturbances and weakness of the legs, succeeded by paralysis, with retention and incontinence of urine and the formation of trophic ulcers. The affection is rapid in its progress and may end fatally in days or weeks.

Chronic syphilitic meningomyelitis is gradual in development, beginning with neuralgic pains in the legs associated with weakness, the patient noticing a curious clumsiness of gait and an inability to run or balance accurately. This is accompanied by difficulty in micturition or nocturnal incontinence and with sexual weakness. Later paralysis and the girdle symptoms and lightning pains of myelitis follow. The affection is slowly progressive.

Most of the myelo-syphiloses show evidences of the syphilitic nature of the affection. In tabes dorsalis no such traces can be found, though the clinical evidence is overwhelming to the effect that the great majority of these cases are syphilitic in nature. It is only in the prodromal period that specific treatment is of avail, and this it usually neglected, being characterized in the main by pains, usually considered rheumatic, urinary troubles, often so slight as to excite little attention, and a moderate but slightly troublesome incoördination in the use of the leg. The Argyll-Robertson pupil is an early and fairly constant symptom, though it occurs in myelopathies other than locomotor ataxia.

Syphilitic neuritis is prone to involve the sciatic nerve and is usually associated with evidences of degeneration, since there is a distinct infiltration, producing pressure. The symptoms are those of neuritis and are intractable in direct proportion to the period of time which has elapsed from the early constitutional outbreak.

HEREDITARY SYPHILIS.

This and the maternal form of the disease are the only ones in which the affection does not begin as a chancre. The term hereditary syphilis implies infection of the ovum before impregnation through the agency of the mother's blood, of the ovum at the time of impregnation by the syphilitic spermatozoön of the father, or of the fetus after impregnation through the placental circulation. It is the disease which kills most infants and produces most abortions (Fournier).

The father will not transmit syphilis through the agency of the spermatozoa during the primary or early secondary incubation periods, though he may and probably will directly infect the mother. Even during an untreated florid secondary period he may procreate healthy children, though he is more likely so to do if he is under an active mercurial medication. Fournier states that true syphilitic symptoms are observed in only 18 per cent. of children begotten of syphilitic fathers; nutritive changes, however, are observed in 82 per cent., these being parasyphilitic in nature and due to syphilotoxins rather than direct inoculation with the germ. The father who is past the contagious period begets cachectic rather than syphilitic children.

The influence of maternal syphilis on the fetus is far more pronounced than is that of infection inherited from the father. Fournier gives the morbidity as 84 per cent. and the mortality as 60 per cent. Even after the secondary period has passed all danger to infants has not disappeared. Fournier admits the transmission of syphilis to the second generation, stating that those hereditarily syphilitic procreate syphilitic children because of their inherited syphilis. This is denied by Caspari.

A child born of syphilitic parents may exhibit no sign of the disease other than immunity against infection, which is transitory, and therefore proves that the child has escaped infection. It probably has absorbed immunizing substances filtered through an unbroken placenta. More commonly such children exhibit either profound changes in nutrition without symptoms of the secondary disease or develop shortly after birth unmistakable syphilitic lesions. In the former case they probably escape direct infection and are immunized, but have suffered from retarded and perverted growth incident to placental disease and malnutrition or syphilo-toxins. When secondaries develop shortly after birth they have received into the circulation the living germ of the disease.

Hereditary syphilis may develop *in utero* and may run its course before birth. Usually children present florid symptoms within three months of birth. If this period has passed without manifestations of the disease, such children may be regarded as having escaped, though exceptionally at puberty they may exhibit tertiary manifestations.

The prognosis of the disease is favorable in inverse proportion to the time intervening between birth and the development of symptoms.

The fetus or still-born child which perishes because of hereditary syphilis will commonly exhibit one or often all of the following signs of the disease: Osteochondritis, enlargement of the liver and spleen, interstitial pulmonitis, cutaneous lesions (particularly bullæ), arachnoiditis, with hydrocephalus and arrested development.

A child carried to full term develops within three months, usually three weeks, one or more of the following signs: snuffles and hoarseness of the voice, eruptions on the skin and mucous membrane, splenic and hepatic enlargements, iritis, cachexia with infiltration of the epiphyseal junction of one or more of the long bones.

After infancy the diagnosis of syphilis will be based on the history of arrest of development and on the traces of former lesions, such as frontal and parietal bosses, flat nose, coryza, corneal opacities, deformity of the tibia, thickening of the long bones near their ends, pharyngeal or palatal ulcerations, deformities of the teeth, linear cicatrices about the lips and nostrils, scars the result of ulcerating syphilides, particularly about the nose and gluteal region, a history of painless otorrhea in childhood, or sudden and complete deafness without otorrhea.

The skin and mucous membrane lesions correspond in type to those observed in the adult and are commonly associated with the weazened, yellow, loose-skinned type of child generally regarded as typifying the effects of hereditary syphilis. Macular eruption is a comparatively rare phenomenon, appearing as large brownish spots prone to desquamate and become moist. Papular eruption is much commoner. It is rarely general, but exhibits a tendency toward grouping and coalescence. In moist regions these papules are converted into mucous patches. About the angles of the mouth they are prone to form cracks and fissures. They are noted particularly upon the buttocks and in the palmar and plantar regions.

The bullous lesions denote a severe infection and may be found at birth. The bullæ are filled with sero-pus and are followed by deep ulcers which become encrusted. They are common on the palms and soles. These bullous lesions at times become filled with blood and are associated with purpuric splotches, constituting hemorrhagic syphilis and much resembling hemophilia.

Mucous membrane lesions cause the snuffles and hoarse voice so characteristic of syphilitic involvement. They may reach a stage of development which seriously interferes with respiration and not infrequently cause pneumonia.

The nails and hair are affected as with the adult.

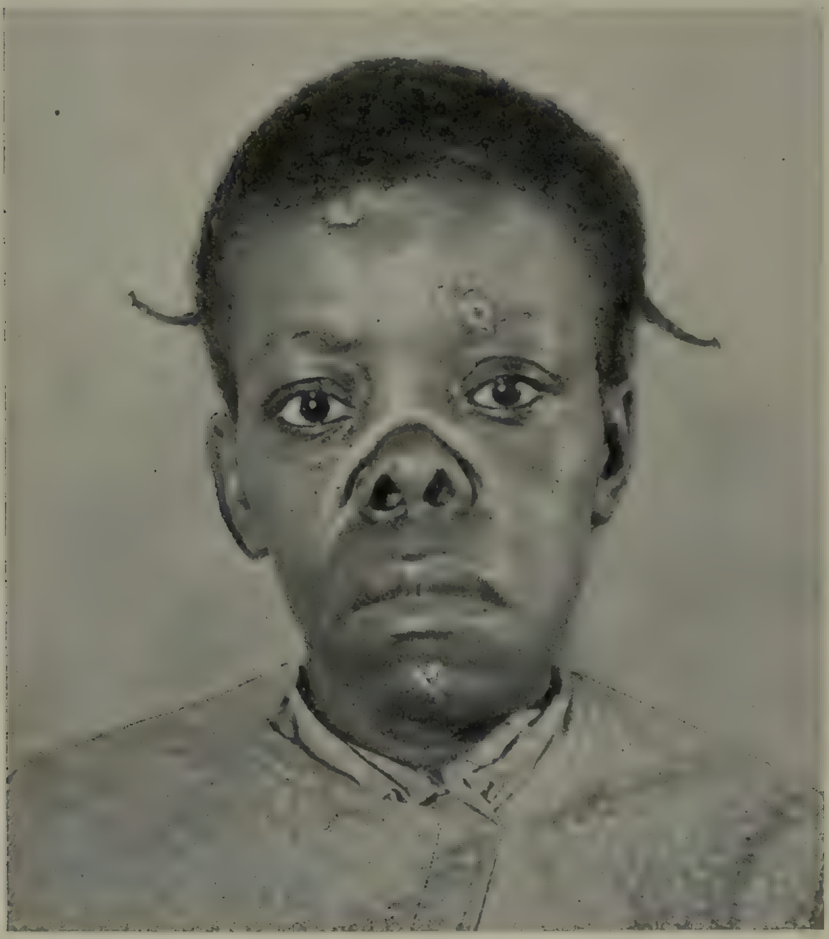


FIG. 185.—GUMMATOUS OSTEOMYELITIS.

The earliest bone manifestation, osteochondritis, usually attacks the radius, ulna, tibia, and femur, though any other bones may be involved, particularly the ribs, sternum, metatarsals, and metacarpals. The affection is characterized by a widening of the cartilaginous plate between the epiphyses and diaphyses, marked by swelling at this junction, often accompanied by moderate synovitis, and, in the absence of treatment, resulting either in softening and separation, characterized by preternatural mobility, or loss of power, constituting the so-called syphilitic pseudo-paralysis.

As a rule, syphilitic bone affections develop after the fifth year, appearing in the form of periostitis or osteomyelitis, usually of the formative type. The frontal and occipital bones are particularly vulnerable, resulting in asymmetry of the skull, bosses or knobs forming.

Degenerative lesions characterized by extensive destruction are common in the nasal bones (Fig. 185). They rarely develop in infancy and are usually due to extension of the disease from the investing soft parts.

The tibia is the one of the long bones most commonly affected. The deformed sabre-shaped tibia is so characteristic as to constitute an important sign of hereditary syphilis.

Syphilitic dactylitis is, as a rule, due to osteoperiostitis, though it may begin in the periarticular soft parts. It forms fusiform swellings, usually multiple and painless, exhibiting ultimately a tendency to break down, exposing necrosed bone and disorganized joints.

Lesions of the brain and spinal cord are similar to those of the acquired disease and are particularly characterized by palsy.

Syphilitic children coördinate badly, are slow in their mental processes, lack self-control, and have defective vision. Headache, epileptiform convulsions, idiocy, paresis, and hemiplegia are common symptoms and sequels of cerebral hereditary syphilis.

Syphilitic children are particularly prone to bronchopneumonia and commonly exhibit enlargement of the liver; albuminuria is fairly common. During the first year of life there is often painless enlargement of the testicles, followed by atrophy.

The parasyphilitic phenomena observed in children who have not inherited the active disease but who suffer from the nutritional starvation or perversion incident to the action of syphilo-toxins either upon the mother, upon the placenta, or upon the fetus, are anomalies of the teeth, imperfect or abnormal development of organs or tissues or general arrest of development, adenoids, rickets, scrofulosis, hydrocephalus, meningitis, epilepsy, hysteria, neurasthenia and idiotism, tabes, and Little's disease.

Abnormalities of the teeth are expressed by tardy development, either of one or more groups or of all, and affecting the eruption of both the temporary and permanent set, arrest or perversion of growth, modification of structure and marked vulnerability, manifested by extensive and rapid caries. Enamel erosion of the cutting edges of the permanent central incisors, forming semilunar notches in small, peg-shaped teeth pointing toward each other, constitute the Hutchinson teeth. Fournier regards an enamel erosion of the first molar as highly characteristic of syphilis. A stump of dentine emerges from the tooth apparently healthy for two-thirds of its height. When this stump is worn down there is left a flat dentine surface bordered by an enamel rim.

It is well established that conditions other than syphilis, such as rickets, mercurial stomatitis, or infantile gingivitis from any cause, may result in similar imperfect development, and that the so-called Hutchinson's teeth are not necessarily characteristic of syphilis.

Kirmesson in 23 cases of harelip was able to obtain a history of hereditary syphilis in 8. Palpebral malformations and deformities about the eye are common. Deformities of the ear or complete absence may be noted. Spina bifida, epispadia, hypospadia, ectopy, cryptorchidism, rudimentary or infantile uterus, infantilism, ascribed by Hertoghe to the influence of syphilis on the thyroid, feminism, acromegaly, rickets (Fournier), anemia, hemorrhagic diathesis, sudden death without cause, one and all are common expressions of the effect of syphilotoxins.

Cerebral lesions developing either in the fetal period or during the first year of life in the centers of association always cause idiocy. Fournier collected 170 cases of hydrocephalus, all due to inherited syphilis. Little's disease is characterized by spastic rigidity accompanying a more or less pronounced paralysis, especially involving the lower extremities, though the upper extremities are sometimes attacked or even the muscles of the trunk, in such wise that the infant lies quite stiff on the knees of its mother. This is a congenital spastic palsy, usually not observed until the child begins to walk.

TREATMENT OF SYPHILIS.

Prophylaxis.—Since syphilis is mainly acquired during illicit intercourse, it is obvious that its prevention would be most efficiently accomplished either by the establishment of a high standard of morality or by stringent enforcement of sanitary regulations bearing not only upon prostitutes but upon men who seek their company. Though efforts have been made in both these directions, the results have not been satisfactory. The very fact of legislating for harlots legalizes the practice, and moreover gives a sense of security to those seeking their company which has not been justified by the results of the most carefully conducted sanitary inspection and control.

Probably the most efficient means of lessening the truly appalling prevalence of the disease is to be found in educating the community as to its dangers. From the scientific standpoint it seems incredible that syphilis, which yearly cripples and destroys more of the vigorous and able-bodied than all the acute exanthemata combined, is an affection of which the carefully reared girl or boy has never heard. When every high school and college has its course of study upon contagious and preventable diseases, including among these syphilis, the first step toward a far-reaching prophylaxis will have been taken.

Since the inoculation of the disease requires contact of the virus with a break in the surface of the unimmunized person, the prophylaxis is comparatively simple. Certainly in the vast majority of cases even though this contact has taken place an immediate cleansing with strong antiseptic solution, preferably pure carbolic acid, is an efficient preventive, though there are recorded cases which tend to prove that such cauterization must take place within a few minutes of the inoculation.

Extragenital chancres are commonly acquired by a lack of cleanliness. They are commonest in medical men and are usually upon the fingers or upon the parts reached by the fingers. They are due to making examinations without properly protecting abraded parts with rubber cots or gloves.

Chancres about the lips or in the mouth are, as a rule, conveyed by patients suffering from mucous patches and quite ignorant of the fact that the secretion from these patches is highly contagious. The prophylaxis here lies in impressing upon each patient suffering from syphilis the nature of the precautions to be taken against infecting others. There are a sufficient number of cases of chancres occurring about the lips or mouth of babies due to kissing of the latter by infected people to demonstrate the importance of protecting children from this to them most unpleasant manifestation of affection.

Fournier calls attention to the fact that hand-made cigars and cigarettes may be sent from the factory bearing the contagion of syphilis.

The lips should be guarded against contact with surfaces which may have become soiled with saliva. Common carriers of syphilis have been drinking-cups, spoons, pen-holders, pencil stubs, pipes, cigars, and cigarettes.

Since the barber shop has many times been responsible for carrying the contagion of syphilis, it is important that such legislation should be enacted as will force barbers to sterilize their instruments after each use. This particularly applies to the alum stick which is habitually employed for the checking of hemorrhage, and which is perhaps more prone than any other implement to carry syphilitic infection.

Excision of the Chancre.—Since syphilis is a constitutional disease spreading from a focus of infection, this focus—the chancre—should be treated by prompt excision. This should be done not so much with the idea of aborting syphilis, though there are a sufficient number of cases recorded to suggest that this may be possible, as for the purpose of lessening the quantity of the infective material. This excision should be practised only when the chancre is so placed that its removal by the knife will not leave a disfiguring or incommoding scar. It should be carried out as soon as the probable diagnosis is formulated, that is, as soon as it is obvious that a lesion developing more than twelve to fifteen days after exposure is not a herpetic lesion or a simple ulcer.

Since this excision can be practised painlessly by local infiltration with eucain, there is no logical reason why it should not be habitually done. Especially so since a microscopic examination of the excised lesion will probably establish the diagnosis.

The moment the probable diagnosis is formulated mercuric treatment should be instituted. During the entire course of syphilis mercury should be the basis of treatment, supplemented by iodids at the end of the second year or at a much earlier period if precocious tertiary symptoms develop. The treatment should continue for four years at least, and thereafter spring and fall for many years, perhaps the entire lifetime of the patient. It should be so conducted as not to interfere with bodily health.

The mercuric treatment should not be pushed even to the first stage of intoxication nor, save in exceptional instances, should the iodid be administered until constitutional effects of the drug are noted.

Of equal importance with the drug treatment is that which has for its end the attainment of the highest possible degree of bodily health. Aside from a disappearance of the obvious lesions of the disease, the best gage as to the efficiency of treatment is to be found in the patient's general condition as evidenced by his own sensations and by his body weight.

General Hygienic Treatment.—On the first suspicion of syphilitic inoculation the patient should have his teeth put in perfect order, should eschew rum and tobacco, and regulate his work, diet, exercise, and sleep as carefully as though he were preparing for an athletic contest which required the highest perfection of physical condition. This in the case of those not previously healthy may require the administration of tonics, stomachics, antirheumatics or other drugs.

The health of the kidneys is particularly important, since to those suffering from nephritis it is extremely difficult to administer efficient doses of mercury without producing salivation or impairing their general health.

Mercuric Treatment of Syphilis.—Mercury exerts a specifically curative effect upon syphilis. The proper dose is that which absolutely controls the disease and is compatible with perfect health. This dose varies not only for each individual but for the same individual at different times.

Loss of weight, general debility, and anemia may be caused by syphilis not controlled by mercury, or by an overdose of the drug. This will have to be determined by noting the effect of temporarily stopping treatment.

The dose is always inadequate when lesions of the disease appear. When tonic treatment is indicated the hypophosphites, iron, and cod-liver oil are most serviceable. The iron and cod-liver oil must be given in a form acceptable to the stomach. It is always in excess when even the slightest symptoms of mercuric intoxication develop. It can be assumed that the proper dose is being given when the patient is in perfect health and absolutely without symptoms of syphilis.

Mercury may be administered by the skin, by the mouth, by hypodermic injection, or by intravenous injection.

Of these various methods its administration by means of inunctions supplemented by vapor, hot-water, or hot-air baths is most efficacious.

Next in order of efficacy is its administration in the form of hypodermic injections. Administration by the mouth comes third, and is the form usually ordered, since it is most convenient and least expensive both as to time and money. Moreover, it is, as a rule, efficient. Intravenous administration is not without danger to life and has not proved for itself a superior efficiency.

Inunctions.—The special value of the inunction method of administering mercury is suggested by the fact that in all the great centers which have acquired a reputation for the cure of recurring and inveterate cases of syphilis this is practically the sole means of administering the drug.

The objections to the method are the time and trouble and exceptionally the publicity incident to its employment.

It has, however, counterbalancing advantages. The dose can be accurately graduated and promptly reduced or increased. It does not, at least by direct action, irritate either the stomach or the bowels and is usually well tolerated by the skin. Exceptionally patients are found in whom its use produces a dermatitis of such severity as entirely to preclude its employment. Most patients can rub in without local ill effect the officinal mercurial ointment provided it has been freshly prepared. This, if too irritating, may be diluted by an equal part of carbolized cosmoline. A serviceable prescription is as follows:

℞. Ung. hydrarg.
Ung. petrolei carbolat........................āā 1 oz.
M. Divide in eight parts, placing each in wax paper or a cachet.
S.—Use one as a surface application immediately after a hot bath.

The usual dose for a healthy adult is 1 dram a day of the undiluted ointment, continued for eight to twelve days, with an interval of rest of two to six days. The patient should be instructed to take a hot-water bath, or better a hot vapor or air bath, until free perspiration is established. In the latter case the bath should last not less than ten or more than fifteen minutes; whereupon he wraps himself in blankets for a further period of fifteen minutes, dries himself thoroughly with a coarse towel, rubs in the ointment for a period of five minutes over an area four times the size of the hand, and puts on a moderately thick undershirt. This is done at night before retiring, and over the undershirt he puts the usual night-garments. The following morning the usual bath can be taken. This should be repeated for eight or twelve nights, a fresh area of skin being selected for each inunction in such manner that the portion utilized for the first treatment does not receive another application for six days. By selecting the areas on the two sides of the anterior surface of the chest and abdomen and in the lumbar region this may be readily accomplished. The inner and outer surface of the thighs and the legs may also be used, in this case the patient wearing a pair of thick drawers beneath his night-garments, thus protecting the latter from staining. Usually the trunk will afford an ample surface.

The under-garments thus worn become thoroughly impregnated with the mercury, and should be preserved and used for as long a period as possible, since the amount of the drug absorbed is thus materially increased. The sweating baths are powerful adjuvants to this treatment and may be administered readily by one of the various cabinets arranged for this purpose. They accomplish a rapid elimination of mercury, thus enabling larger doses to be used without deterioration of general health.

The gage as to the efficiency of the treatment will be the disappearance of symptoms. If under the use of a dram a day rapid resolution occurs, the dose may be considered adequate. If, however, the lesions are tardy in disappearing or show but little improvement, the dose should be increased to two, three, or exceptionally four drams a day.

An effort should be made to avoid even the first sign of salivation. Should symptoms of this condition develop the mercury should be stopped, but the vapor baths should be continued, since these are the most powerful stimulants of elimination of the drug.

The average dosage is subject to so many individual exceptions that it is of little service in formulating a treatment. For the first year of the disease most patients can take the equivalent of a dram of mercury ointment a day for six to ten days in succession, followed by a rest period of three to five days. The dose may have to be doubled or quadrupled, with shortened rest periods. Exceptionally a half a dram a day for not more than three to five days in succession represents the maximum helpful dosage. As the disease grows older the treatment periods should be shorter, the rest periods longer; six days of rubbing and six of rest for the second year, six rubbing days and twelve rest days for the third year, and six rubbing days with eighteen rest days for the fourth year, will represent about the average.

During the spring and fall of the third and fourth years the doses should be increased for one month. After the fourth year in the absence of tertiary symptoms two series of twelve inunctions with six days' rest between may be ordered spring and fall for four more years.

When tertiaries develop in the absence of such treatment or in spite of it, the mercury should be continued for two years, as in the second year of the disease. Even if patients be unable to take the inunction treatment in its entirety it serves as a useful adjuvant to the administration of the drug by the mouth, the latter being discontinued for six days of the month, during which period the patient takes the mercury ointment and the vapor bath.

Hypodermic Injections.—This method of treating syphilis has for its most conspicuous advantages prompt absorption, precise dosage, and the avoidance of irritating effects upon the gastro-intestinal tract. In its application it is usually painless and unattended by inflammatory reaction. Unfortunately it is at times attended by such severe pain as entirely to cripple a patient for several days. Such a mischance cannot be predicted and cannot be avoided, and may suddenly occur in a patient who has previously taken dozens of such treatments without ill effect. Also, it is responsible for a number of cases of fatal salivation, since the absorption is rapid and cannot be at once controlled. This is particularly the case when insoluble preparations of mercury have been used. As to cellulitis and infection, these can be avoided by cleanly methods, and hence do not constitute an essential objection to the method.

The drugs used may be either in a soluble or an insoluble form. The injection in either case must be accomplished with perfect cleanliness. This, of course, implies, in addition to the preparation of the skin, the boiling of the needle and the syringe. The ordinary hypodermic answers well, provided it be cleansed immediately after use. For the insoluble preparations a needle with a rather large lumen should be employed.

The post-trochanteric, the lumbar, and the upper dorsal regions are those usually selected for injection, the drug being driven into the muscular tissue. The needle is disconnected from the syringe, thrust in deeply, and allowed to remain for a moment to determine whether or not it has punctured a vein, since injection in such cases has resulted fatally. In case no blood flows, the syringe is attached to the needle and the injection is driven in. The injection point should be kept covered for a moment with sterile gauze. It requires no further dressing.

The ordinary dose of the corrosive chlorid of mercury is from $\frac{1}{12}$ to $\frac{1}{3}$ of a grain. This is injected daily, since the absorption is rapid, and must be repeated in appropriate doses until the symptoms disappear, after which time it is continued in series of six doses with intervals of six days' rest for the first year, and in series of three doses with intervals of nine days' rest for the second year, the quantity being increased or diminished in accordance with the clinical indications.

These injections are particularly indicated when the inunction treatment is not applicable and when the administration of mercury by the mouth is contraindicated by intercurrent gastro-intestinal disturbances. They are also indicated for the cure of syphilitic lesions which threaten life or function in their development, or in which an early differential diagnosis is imperative, as in case of gummata simulating malignancy.

A serviceable formula for the hypodermic administration of corrosive mercuric chlorid is as follows:

Corrosive mercuric chlorid	$4\frac{8}{10}$ grains
Sodium chlorid	$3\frac{1}{2}$ grains
Distilled water	f℥j

S.—Ten to 30 minims hypodermically.

A stronger solution than this may cause local necrosis; a weaker one requires too bulky an injection.

Calomel still remains the favorite form of mercury for the insoluble injections. The advantage incident to its use is dependent on the fact that it remains long in the tissues and is slowly absorbed, hence comparatively few injections are required, and these may be given with long intervals between.

A convenient formula is the following:

Calomel	1 part
Fluid cosmoline	4 parts

This mixture should be subjected to the temperature of boiling water before being used and 5 minims should be injected deeply, precaution being observed, as above advised, against puncturing a vein. One grain of calomel may thus be injected four times a month, the dose again being increased or diminished in accordance with the indications (disappearance of symptoms and perfect health of the patient). Taylor warmly commends yellow oxid of mercury as a most serviceable form for the injection treatment. When insoluble preparations of mercury are employed the site of injection must be accurately recorded, so that the surgeon, in case of beginning salivation, may at once cut down upon the seat of the last injection and mechanically remove all the drug that has not yet been absorbed.

Administration of Mercury by the Mouth.—The great advantage incident to this method of administration is its convenience, the patient being required simply to swallow a tablet three to six times daily. It is also, as a rule, an efficient method, since most of those afflicted with syphilis who are thus treated recover promptly and do not exhibit late recurrences, hence it will undoubtedly remain the method of choice in the majority of cases.

The objection incident to it is that it often exerts an irritating effect upon the gastro-intestinal tract, and that possibly owing to this or to changes in the conditions governing absorption the amount of mercury actually taken into the system is subject to wide variations, even though the same dosage be continued. It thus happens that a patient who is daily taking a grain and a half of the yellow iodid of mercury may without fluctuation in the quantity ingested exhibit in one month lesions of syphilis, proving that the dosage is insufficient, while in the next he may develop salivation, showing that the dosage is excessive. It is in such cases that the oral administration of mercury is least successful.

Where mercury can be taken by the mouth in sufficient quantity to cure the lesions of syphilis and prevent their recurrence without causing gastric or intestinal disorders, there can be no objection to this method of using the drug. However, if the patient's appetite fails, if he loses in general condition and is subject to recurrent manifestations of syphilis in spite of what seems to be an adequate dose of mercury by the mouth, the inunction treatment or, if this be impossible, the hypodermic administration of mercury should be adopted.

The form of mercury given by the mouth must vary somewhat with the individual. As a rule, the yellow mercurous iodid will be found most serviceable. This may be administered in tablet form after meals. The ordinary dose is one-third of a grain three times a day; twice or four times this quantity may be required. Exceptionally not more than one-third of a grain twice a day will be tolerated. Patients who cannot take this form of mercury without experiencing colic and diarrhea can often take a grain of mercury and chalk without local ill effect. Exceptionally $\frac{1}{12}$ to $\frac{1}{15}$ of a grain of bichlorid of mercury will prove less irritating.

The gage as to the dose of mercury is the disappearance of specific symptoms. This dose must be varied from time to time lest the drug itself produce deleterious effects. The patient should not lose in weight without apparent cause and he should feel well.

In patients who tolerate the oral administration of mercury, whose health remains unimpaired, and who exhibit no recurrences the treatment should be a continuous one for two years with one or two rest days in each week. It should be intermitted one week in a month in the third year, two weeks in a month in the fourth year, and should be continued spring and fall for at least one month for the next four years. A recurrence at any period of the disease should be followed by continuous treatment for one year and interrupted treatment for the second year. During the whole of this period the patient must be most carefully guarded against the toxic influences of the drug.

Hydrargyrism.—Mercury may exhibit its toxic effects either in the acute or chronic form. There is at times an extraordinary susceptibility to the drug.

Acute hydrargyrism in its mild form is characterized by fetor of the breath, metallic taste in the mouth, increased flow of saliva, tenderness of the teeth, and spongy, readily bleeding gums. In its more severe form the symptoms are all accentuated, the gums much swollen, the teeth loosened, and the whole mucous membrane of the mouth edematous, congested, and eroded. The flow of saliva is profuse and distressing. The breath is conspicuously foul and the glands beneath the jaw and in the neck become swollen. The mouth and teeth are so tender that mastication is difficult or impossible.

Associated with these symptoms there may be colicky pains, bloody stools, and blood and albumin in the urine. These latter symptoms may develop in the absence of mouth symptoms, and should always be looked for in persons with crippled kidneys to whom mercury is given.

Exceptionally the drug manifests its toxic symptoms in the form of a dermatitis, which is then an expression of idiosyncrasy.

Chronic hydrargyrism is characterized by symptoms of chronic gastro-enteritis attended by failure of appetite, progressive weakness, emaciation, often albuminuria, and as a rule profound mental depression with neurasthenic symptoms. Precisely these same symptoms may develop as the result of inadequate medication.

Mercuric intoxication is avoided by careful attention to the dose and by encouraging free elimination by the bowels, kidneys, and skin. On the first symptom of its development the mercury should be stopped and sweat baths should be given. These may be supplemented by a tincture of myrrh wash, painting the inflamed gums with 5 per cent. solution of protargol, the use of a cocain spray before administering food to lessen the pain of its mastication and deglutition, and by small doses of atropin.

Chronic hydrargyrism is best treated by the withdrawal of mercury and the use of sweat baths. General tonic and hygienic treatment is indicated, together with change of air and surroundings.

Treatment by Iodids.—Iodids in the early stages of syphilis, except when this is characterized by lesions of the late type, are of no value. In the later stages, particularly when these are manifested by infiltrations of the central nervous system, they powerfully stimulate absorption.

It is usual in the systemic treatment of syphilis to begin the iodids after eighteen months, administering in the absence of symptoms, 5 grains three times a day after meals. When mercury is given by the mouth they may be advantageously combined with this drug in the form of a tablet, each to contain 2½ grains of potassium iodid and $\frac{1}{24}$ of a grain of corrosive mercuric chlorid. Two of these tablets may be taken after each meal, the dose of each ingredient being varied to suit the case.

It is customary to give the iodid in liquid form, so put up that each drop of the solution equals approximately one grain of the potassium iodid.

Potassium iodid.................................3℥
Distilled water, q.s...............................f℥j
S.—Five drops or more three times a day given in a full glass of water or milk.

Sodium iodid is at times better tolerated than the potassium salt, and may be given in the same dose as the latter.

The objection to the iodids is incident to the fact that they have an irritating effect upon the stomach, and in some persons even in small doses produce symptoms of iodism.

The effect upon the stomach may be obviated almost entirely by giving the iodids in wide dilution. Milk as a diluent is particularly serviceable since it entirely covers the disagreeable taste of the drug.

Probably the most efficient and least disagreeable way of administering potassium iodid is by adding the number of drops of the saturated solution required to a glass of milk, which is then converted to a junket by the addition of essence of pepsin and is agreeably seasoned. This may form part of the meal.

As a rule, the drug should not be given to the extent of causing iodism. For the combating of late infiltrating lesions, particularly such as involve the integrity of the central nervous system, it may be needful to push the iodids to the extreme limit of tolerance, giving enormous doses.

Tolerance to iodids is of no diagnostic value in so far as syphilis is concerned, nor does susceptibility to small doses always imply that full doses should not be given in case of need. An ounce of potassium iodid has been given as a daily dose with advantage to the patient.

Iodism.—Iodin manifests its constitutional symptoms in the form of gastro-intestinal disturbances, coryza, pustular skin eruption, lacrymation, tinnitus aurium, and mental depression. Acute neuritis has been noted, and still more exceptionally sudden edema of the larynx, the latter from very small doses of the drug and as an expression of idiosyncrasy.

The usual eruption is acniform, though exceptionally the dermatosis may simulate almost any form of skin disease. Sometimes it is destructive in type.

One or more of the symptoms of iodin may develop in the very beginning of treatment, and if mild in type do not necessarily constitute an indication for suspension of the drug, since in the majority of cases a certain tolerance is established.

Fowler's solution administered in small doses with the iodids seems to have a beneficial effect in preventing the specific symptoms incident to the ingestion of iodin. Belladonna is alleged to have the same effect.

Gastro-intestinal symptoms are avoided by giving the drug in wide dilution after meals.

Treatment of Hereditary Syphilis.—Prophylactic treatment lies in discountenancing marriage on the part of those who have had syphilis until the disease is at least four years old and has shown none of its manifestations for a full year. During this time the patient should have been subject to a thorough mercurial treatment. In the case of pregnancy occurring when either of the parents is syphilitic the mother should be subjected to a vigorous mercurial treatment, supplemented by tonics, special care being taken to avoid irritation of the gastro-intestinal tract.

A child born of syphilitic parents is not necessarily syphilitic, hence mercuric treatment should not be instituted till symptoms develop. The dystrophy which such children exhibit may be parasyphilitic and will be made worse by active mercurial treatment. The nutrition of such children should receive especial attention, since they are, as a rule, more or less cachectic. They should be breast-fed and the nurse should be the mother or a woman certainly immune against contracting the disease.

Iodid of iron, cod-liver oil, and hypophosphites are particularly serviceable.

When the unmistakable lesions of the disease appear, the mercurial treatment is best applied by means of a mercurial ointment diluted with three parts of vaselin. This is spread on the child's binder in the dose half a dram a day. The skin to which the application has been made is thoroughly washed with soap and water at the end of each twenty-four hours and bathed with boric acid solution. This flannel binder is changed for a clean one every fourth day. In case dermatitis develops, other surfaces of the body must be used, or the mercury may be rubbed in as in the case of an adult. The proper dose is that which causes prompt subsidence of the lesions and does not interfere with general health.

Exceptionally the skin is too tender to tolerate any surface application of mercury. Hypodermic injections may then be employed, the solution of choice being the 1 per cent. sublimate mixture, of which 1 to 4 minims are given every second day. If this method is contraindicated calomel may be given by the mouth from $\frac{1}{10}$ to $\frac{1}{5}$ grain thrice daily.

Mercurial treatment should be continued with increasing periods of rest until after the age of puberty. The iodids are of little service and are prone even in moderate doses to cause iodism. In lesions of the bones, central nervous system, and viscera they have their most useful application, and infants may be given from one to three grains daily. An efficient treatment cures the lesions of syphilis and betters the general health of the child. The dose of mercury which accomplishes these results must be found by careful trial.

If coincident with the disappearance of the syphilitic manifestations the child grows progressively weaker and more anemic, it is probable that it is suffering from chronic hydrargyrism. These same symptoms may be expressions of syphilis inadequately controlled because of a too feeble dosage of mercury.

Local Treatment of Syphilitic Lesions.—The local treatment of syphilitic lesions is conducted on general surgical principles. A vigorous constitutional treatment is the most efficient method of causing resolution. The chancre should be kept clean, protected from friction, and dusted with calomel and bismuth. The erythematous syphilides fade quickly. Papular syphilides, if persistent, may be benefited by general inunction of the affected region with an ointment made up of ammoniated mercury 20 grains to the ounce of cold cream.

Vaporizations of calomel are particularly serviceable for the cure of papulosquamous lesions. Mucous patches may, as a rule, be prevented by local cleanliness and constitutional treatment. When they appear applications of 10 per cent. solutions of silver nitrate supplemented by antiseptic mouth-washes are efficient. If very persistent, iodin 2 drams to the ounce of glycerin may be brushed on.

The opalescent scaly patches which occur late in syphilis are extremely persistent. They are best treated by a brushing with 10 per cent. chromic acid. At times they may require removal with a sharp curette or actual cautery.

Syphilitic vegetations are best treated by chromic or carbolic acid, the former in 50 per cent. solution and the latter pure. Chromic acid may occasion toxic symptoms if applied to a large surface. As a rule, these vegetations readily get well if they are cleansed, dried, and dusted with calomel.

Periosteal nodes are best treated by freezing over them with chlorid of ethyl and applying compound iodid ointment.

Extension of persistent spreading serpiginous ulceration is treated by curettement, cauterization, and prolonged or continuous baths of mild antiseptic solution.

Serum Treatment of Syphilis.—Thus far the serum treatment of syphilis has been richer in promise than in results. With the now well-established fact that the disease is inoculable upon some anthrapoid apes, laboratory research becomes possible, though the results of attempts at immunizing by means of triturates of human chancre have not been promising. The fact that a person with a chancre is immune against the contraction of another chancre by inoculation is highly suggestive. Experimentally, subcutaneous immunization is not available against cutaneous infection, though there is some evidence to show that it may prevent the general infection.

CHAPTER XXI.

TUMORS.

By John Bland-Sutton, F. R. C. S., Eng.,

LONDON.

It has long been customary in surgical writings to group together a very heterogeneous assembly of morbid conditions under the term "tumors"; this is a very ancient name and merely signifies a "swelling," but the careful microscopic investigations of morbid anatomists with the aid of differential staining (histologic chemistry), and the study of the relationship of microörganisms to many swellings called tumors, have led to a revolution in our knowledge, so that the term has been stripped of its former wide significance. In clinical work the word tumor is not likely to disappear, although it has lost its importance to the pathologist.

Formerly the term tumor was applied to the abnormal swellings which characterize the gummatous stage of syphilis, the lesions of actinomycosis, leprosy, and other diseases collectively known as the infective granulomata: the peculiar cystic swellings produced by the embryo of *Tænia echinococcus;* the excessive formation of callus around the broken ends of bones, and the exuberant production of cicatricial tissue known as keloid. It is noteworthy that almost every increase in our knowledge regarding the cause of these tumor-diseases results in reducing the list of morbid conditions known as tumors, either by removing some from this category altogether, or by combining under one term a number of apparently diverse conditions which were formerly regarded as independent. Tumor-diseases of the nervous system are a striking illustration of this. Among recent evictions from tumors is the enlargement of the prostate in advanced life, which is usually classed with adenomata, but some excellent observations have been conducted into the cause of this trouble (the bane of elders) which indicate that it is due to infective agents which gain access to the glandular recesses of the prostate from the urethra and set up inflammatory (reactive) changes. Being ignorant of the cause of tumors (pathogenesis), we fall back on their minute structure (histology) as a scientific basis of classification. This method was the natural outcome of the careful investigation of the histology of tumors, because it led investigators to realize that they consisted of the same tissues which compose the normal organs of the body. This was a great step. Anatomic observations taught men that their bodies are made up of many diverse structures, such as fat, suet, gristle, bone, muscle, tendon, and the like, but the microscope revealed that they are composed of fundamental tissues which enter into the construction of organs of the most diverse form and function. The basis consists of connective tissues comprising bone, fat, cartilage, etc., and two remarkable structures known as muscles and nerves. There is also the peculiar material which permeates the body and enters into the composition of every organ, called areolar tissue, a ubiquitous web which is stout and strong as fascia and periosteum, extremely delicate in the nervous system, and so fine in the retina that it needs careful preparation to render it perceptible to the microscope. The connective tissues form the framework of the body and constitute a sort of sustentaculum in the compound organs, such as the liver, intestines, kidneys and the like, for the support of epithelium, and act as a mesh in which blood-vessels and lymphatics can ramify to supply the liquid tissue—blood, from which the epithelial cells can obtain material to form the secretion characteristic of the particular gland to which they belong.

The careful and critical study of the minute (microscopic) structure of tumors having revealed that they were composed of tissues normally existing in the body, pathologists realized that the structure of a tumor invariably corresponded with that of the tissue in which it grew: thus a fatty tumor arises from fat, an osseous tumor from bone, and so on. This is known as the "law of prototypes," and a careful study of it enables pathologists to predict the various primary tumors to which an organ may be liable, as well as to explain why tumors containing epithelium do not arise primarily in bone or muscles, or odontomes in the liver or myomata in the brain.

It may be stated without fear of contradiction that no one has succeeded in framing a satisfactory classification of tumors. In the present article the following plan will be followed:

Group I. Tumor-diseases of the Connective Tissues. This will include: Lipomata; Chondromata; Osteomata; Myelomata; Fibromata; Sarcomata; Angeiomata; Lymphangeiomata; Endotheliomata; Fibroids; Neuromata; Myomata and Myxomata.
Group II. Tumors-diseases of Teeth; Odontomata.
Group III. Epithelial Tumors. This comprises Papillomata (Warts); Adenomata; Carcinomata.
Group IV. Tumors arising from fetal membranes: Chorion-epitheliomata.
Group V. Teratomata, Dermoids and Embryomata.
Group VI. Cysts.

Tumors have from very early times been arranged into a malignant and an innocent or benign division, based on the knowledge gained from observation that some of them inevitably destroy life while others do not display such destructive propensities. This division is sound because malignant tumors belonging to the connective-tissue group (sarcomata), as well as those of the epithelial group (the carcinomata or cancers), present structural peculiarities which enable competent histologists to recognize them.

It is important to remember that benign tumors may and often do destroy life. The essential difference between an innocent and a malignant tumor may be expressed thus: *The baneful effects of innocent tumors depend entirely on their environment, but malignant tumors destroy life whatever their situation.*

There are some anatomic conditions which distinguish innocent and malignant tumors. Those that are benign usually possess an investing envelope known as a capsule by which they are isolated from the tissue in which they grow; they do not infect the lymph glands, nor recur after complete removal, and they rarely imperil life save when growing in connection with, or in the immediate vicinity of vital organs. Malignant tumors, on the other hand, are rarely encapsuled, and tend to infiltrate the surrounding tissues; they infect the lymph glands which receive the lymphatics from the part affected; are exceedingly liable to recur after removal, tend to become disseminated by the lymph and blood stream, and inevitably destroy life.

Malignant tumors of the connective-tissue group are known as sarcomata; those arising from the blood and lymph vessels are called endotheliomata. Among the epithelial group carcinomata (cancers) and chorion-epitheliomata are excessively malignant, and the malign examples among the dermoid group are termed malignant embryomata.

It is a feature of benign tumors that they are apt to be multiple; for example, fatty tumors, cutaneous neuromata, fibroids, chondromata, osteomata, etc.; but the occurrence of two primary cancers is excessively rare. The coexistence of two varieties of simple tumor is not rare, and an organ which is occupied by an innocent tumor may also become the seat of malignant disease (cancer). Uterine fibroids and cancer of the uterus is a not infrequent combination.

The Transformation of Innocent into Malignant Tumors.—A long study of the histogenesis of tumors has convinced me that the clearly innocent and the decidedly malignant tumors present distinct histologic features, but there are intermediate varieties which cannot be sharply defined in relation to these points, and this comes out in a striking and suggestive way when an individual possesses tumors of a supposed innocent genus in multiples: for example, among uterine fibroids when they are multiple, a tumor may sometimes be selected which requires a saw to divide it; another may be as soft as a ripe fig; and a third will be as viscous as jelly and almost diffluent: a soft fibroid of this character will sometimes recur after enucleation. Careful records are accessible in which fibroids of apparently simple structure have disseminated and destroyed life; it should be borne in mind that the uterus is liable to be the seat of true sarcomata which in the early stages mimic in their naked-eye characters fibroids. It is so difficult to decide between the slow-growing spindle-cell sarcoma, the fibrifying sarcoma, and the gelatinous fibroid (myxoma) that it is unwise to argue from our present knowledge that innocent connective-tissue tumors may undergo transformation into sarcomata until distinctive methods have been introduced by the histologist, chemist, biologist, or the bacteriologist. The more carefully the histology of tumors is investigated, the more obvious does it become that the borderland between innocent and malignant species becomes less easily definable. This has been very definitely revealed in the case of dermoids. Few tumors had a better reputation for innocency, yet we now know that the less typical forms are liable to infect the peritoneum and even disseminate, and some varieties of testicular embryomata are among the most malign tumors that attack mankind. Realizing the uncertainty attending the diagnosis and prognosis of tumors and tumor-diseases, pathology confirms the practice advocated by surgeons in dealing with them: namely, *Removal whenever practicable at the earliest possible moment.*

GROUP I.—TUMOR-DISEASES OF THE CONNECTIVE TISSUE.

Lipomata (Fatty Tumors) and Lipomatosis (Obesity).—Lipomata are encapsuled tumors composed of fat, and they have a distribution in the body as wide as adipose tissue. With the exception of the sarcomata it is the most generalized genus of tumors which occurs in man. Lipomata are very common in the subcutaneous tissue of the trunk and trunk-end of the limbs. As a rule, one tumor is present, but twenty or more may grow concurrently on the same individual. A lipoma of the size of an adult fist is regarded as a tumor of fair size, but it may attain twenty times this dimension. Cases formerly reported in which hundreds of cutaneous tumors existed on one person and the very large pendulous masses of molluscum fibrosum do not belong to the lipomata. (See *Neurofibromatosis.*)

Subcutaneous fatty tumors grow also on the fingers, the palms, soles, and scalp. Lipomata have been known to exist on an individual without causing more than trifling inconvenience for thirty years and more. In old tumors the fibrous septa may calcify and the fat occasionally undergoes saponification. Although these tumors are usually encapsuled, instances are not rare in which they become pedunculated.

The peritoneum, like the skin, rests upon a bed of fat, the thickness of which varies greatly not only in different individuals but also in the subserous regions of the same person. For example, in the renal region fat (suet) is usually very abundant, and in the mesentery and omentum, whereas the subserous tissue beneath the peritoneum covering the liver, uterus, Fallopian tube, and ovary is almost devoid of fat. Encapsuled collections of fat are met with throughout the subserous tissue. When they arise in the mesentery, or in the fat at the base of the broad ligament (mesometrium) or in relation with the perirenal fat, they attain a large size and simulate many forms of abdominal tumors, and have been known to weigh upwards of half a hundred-weight.

When lobulated collections of subserous fat arise in the regions of the inguinal and femoral rings they will protrude externally and draw with them small peritoneal pouches and simulate a hernia, and in cases where hernial sacs already exist a lobule of fat may invaginate it and produce a lipoma in a hernial sac. Small peritoneal pouches accompanying protruding fat lobules are not uncommon in the linea alba. The "fatty hernia" of the linea alba may be subsequently occupied by a piece of bowel and become a true hernial sac.

The fatty lobules on the colon known as appendices epiploicæ may be mentioned in relation with fat-hernia. An appendix epiploica is a fold of peritoneum filled with fat, and its size depends entirely on the amount it contains; the fat of the appendix can be shown by simple dissection to be directly continuous with the subserous fat which normally fills the interspace of the mesocolon, and with care it is easy to show that the serous investment of the colon reposes on a subserous tissue containing varying proportions of fat throughout that part of the circumference of the gut which receives a peritoneal investment.

When a transverse section of the descending colon from a very fat individual is examined the relation of the subserous fat to that of the epiploic appendix and the mesocolon is easily seen. The part of the colon which is most avoided by fat is the middle tænia or longitudinal band; even in very obese individuals this band is rarely obscured.

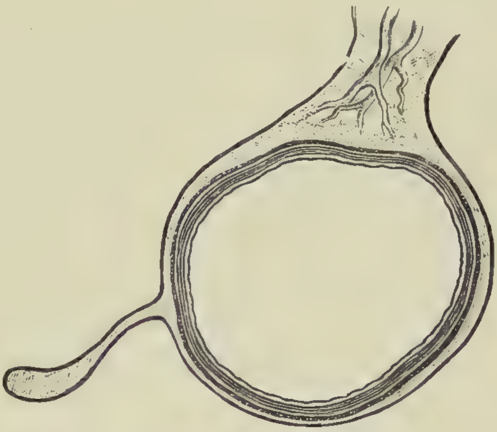


Fig. 186.—Transverse Section of the Descending Colon from a Thin Man Showing the Relation of an Epiploic Appendix to the Susberous Fat.

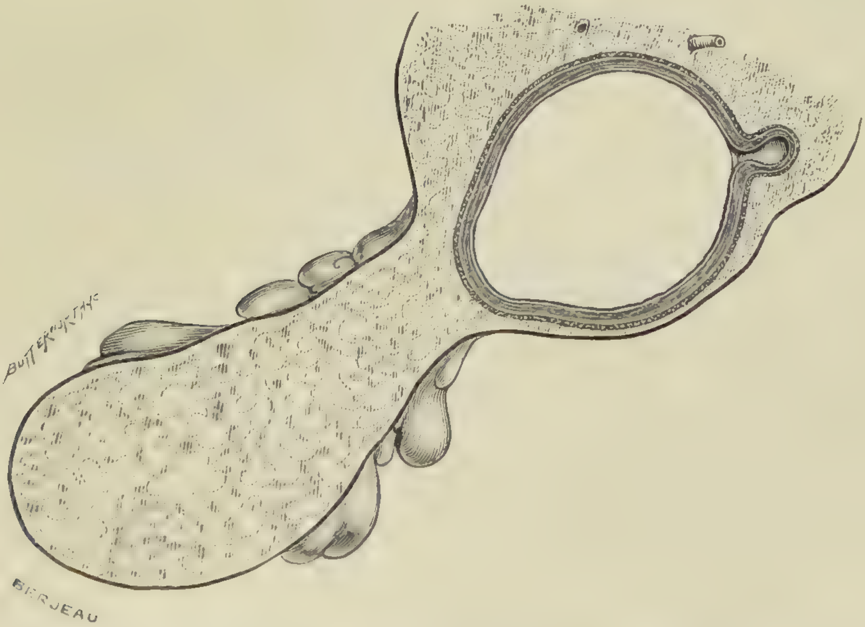


Fig. 187.—Diagram of a Transverse Section of the Colon from a Very Fat Man, Aged Fifty-five Years, to Show the Disposition of the Subserous Fat and its Relationship to the Epiploic Appendage.

In the specimen from which the diagram was prepared a sacculus (or pressure pouch) had been divided in making the section.

In thin persons the connection between the adipose tissue in the mesocolon and the appendices epiploicæ is not so obvious, and in extreme cases the wasting may be so extreme that these fat-appendages may be represented as nodules of fat swinging on slender pedicles, some of which may be tightly twisted. Occasionally these pedicles break and the nodule is set free. Sometimes the fatty lobule is calcified, and hard bodies of this kind are found free in the abdominal cavity and may even find their way into hernial sacs.

It has already been mentioned that lobules of subserous fat may protrude in the neighborhood of the linea alba and drag pouches of the peritoneum with them; in the same way the epiploic appendages may produce small saccules of the colon, especially in obese persons, independent of the normal haustra, and these pouches sometimes lodge foreign bodies which are apt to perforate its walls and give rise to an abscess in the epiploic appendage.

An encapsuled lipoma may arise in the subserous tissue of the intestine and, protruding through the muscular coat, present as a polypus into the lumen of the gut. Tumors of this kind have been observed in the colon (Bland-Sutton, Knaggs) and in the ileum (Stabb): in each instance the lipoma caused intestinal obstruction. The serous surface of the bowel over a lipoma of this character presents a well-marked dimple or depression. Similar fatty tumors have been observed in the stomach (Virchow).

Lipomata may arise from the subserous fat of the pleura, and in one remarkable case the tumor had the shape of a dumb-bell, one end lying beneath the pleura, the other being situated under the pectoralis major muscle, the isthmus passing between two ribs. The subpectoral end of the tumor led to the diagnosis of a sarcoma (Gussenbauer).

Beneath the subserous tissue of large joints, such as the knee, there is a layer of fat of varying thickness. This fat may, as in the case of inguinal lipomata, increase in quantity and, projecting into the joint, form a fatty tumor. A common situation for this to occur is beside the patella, at the spot normally occupied by the alar ligaments. Many specimens are doubtless due to overgrowth of the fat in the alar fringes, but they may arise in other parts of the joint.

The best-known variety of subsynovial fatty tumor is that to which Müller applied the term "lipoma arborescens." This condition is often, but by no means always, associated with rheumatoid arthritis. The lipoma arborescens bears precisely the same relation to the synovial membrane that the appendices epiploicæ bear to the peritoneal investment of the colon and sigmoid flexure.

Among rare situations in which lipomata arise may be mentioned beneath the mucous membrane of the lips, the conjunctiva, the interspaces of muscles, and in the belly of such a muscle as the deltoid or the biceps. Very large encapsuled fatty tumors have been reported growing between the muscles of the abdominal wall. A rarer place is the periosteum of bones, such as the scapula, femur, ischium, tibia, etc. Two important features of lipomata growing from periosteum require mention: they usually contain striped muscle fibers and are congenital in origin. The greater number have been observed in children.

Fatty tumors grow also from the trunks of nerves, such as the median at the wrist and the great sciatic in the ham.

The collection of fat overlying the sac of a spina bifida is sometimes described, but not rightly, as a lipoma; encapsuled fatty masses are found, though rarely, on the dura mater of the spinal cord, and in one carefully reported case a lipoma grew from the dura mater of the sella turcica and extended into the middle fossa of the skull: it was as big as a child's fist. The patient, a woman aged forty-two years, complained of periodic pain in the head and eventually of ptosis.

Lipomatosis (Obesity) and Diffuse Lipoma.—Obesity or the excessive production of fat in the subcutaneous, intermuscular, and subserous tissue is due to the fact that more fat-forming substances are taken as food than can be physiologically utilized in the functions of the organism, and the excess is deposited as adipose tissue, and these fatty deposits are most marked on the trunk, trunk-ends of the limbs, the buttocks and neck, and in the mesentery and omentum. Normally fat is deposited uniformly; exceptionally the deposition occurs irregularly and forms lumps which are known as *diffuse lipomata,* which, as symmetrical swellings in the neck on each side of the ligamentum nuchæ, and especially under the chin, are well known. They are in no sense to be regarded as tumors. This fat has a coarsely granular appearance, due to being bound up in tiny lobules, which causes it to resemble omentum. In the neck these collections of fat are situated on the deep as well as the superficial aspect of the platysma muscle. Similar unencapsuled masses of fat occur in the groin, pubic region, and axillæ.

Clinical Features.—Although lipomata occur more frequently than any other genus of connective-tissue tumor, and may in most instances be diagnosed with certainty, yet under some conditions they are very puzzling, and give rise to much difference of opinion. They may arise at any age and are occasionally congenital. The subcutaneous variety is rarely the source of doubtful diagnosis, unless situated in the palm or the sole, or on the scalp. The intimate relation between the tumor and the overlying skin, the absence of definite boundaries, and its dough-like consistence are usually sufficiently trustworthy guides. When a lipoma is connected with the periosteum of a long bone it will sometimes simulate a sarcoma; when embedded in a muscle or in the tongue the most divergent opinions are often expressed in regard to the nature of the tumor.

A lipoma in the posterior triangle of the neck has been mistaken for an aneurism of the subclavian artery and the vessel ligated in error.

Reference has already been made to those large lipomata which arise in the subperitoneal tissue and the way they mimic the signs of ovarian tumors. Lipomata in the neighborhood of hernial openings have also been confounded with herniæ.

Especial attention must be drawn to supposed fatty tumors situated in the middle line of the back; in most cases these are abnormal masses of fat overlying the sacs of spinæ bifidæ. Incautious surgeons, in operating upon such tumors, have unexpectedly opened the dura mater.

Treatment.—Solitary subcutaneous lipomata should, as a general rule, be removed. When very many tumors are present (ten or twenty) it is not customary to interfere with them, for when multiple they rarely attain uncomfortable or dangerous proportions. It occasionally happens with multiple (and also with solitary) lipomata that one or other becomes irritated with some part of the dress, such as petticoat bands, braces, etc., or in some particular employment followed by the individual. Such tumors should invariably be removed.

The removal of a subcutaneous lipoma is one of the simplest proceedings in surgery, but the extirpation of a large subperitoneal fatty tumor is often attended with difficulty and grave danger.

Lipomata never recur if completely removed; they are dangerous to life only when they grow in the cranium or spinal canal, or when growing from the walls of the intestine and protruding into its lumen, causing intussusception.

Chondromata. (**Cartilaginous Tumors.**)—*A chondroma is a tumor composed of hyaline cartilage and growing from preëxisting cartilage.* The tissue of chondromata resembles histologically the bluish translucent cartilage of an epiphyseal plate.

Chondromata occur in long bones and, as a rule, in relation with the epiphyseal cartilages, hence they are most common in children and young adults. A single tumor may be present, but occasionally many grow concurrently on the long bones of the hands and feet, especially in those who have suffered from rickets, and their frequent association with this disease led Virchow to attribute their origin to untransformed pieces of hyaline cartilage derived from the epiphyseal discs. Such remnants of untransformed cartilage are not difficult of demonstration in rickety bones.

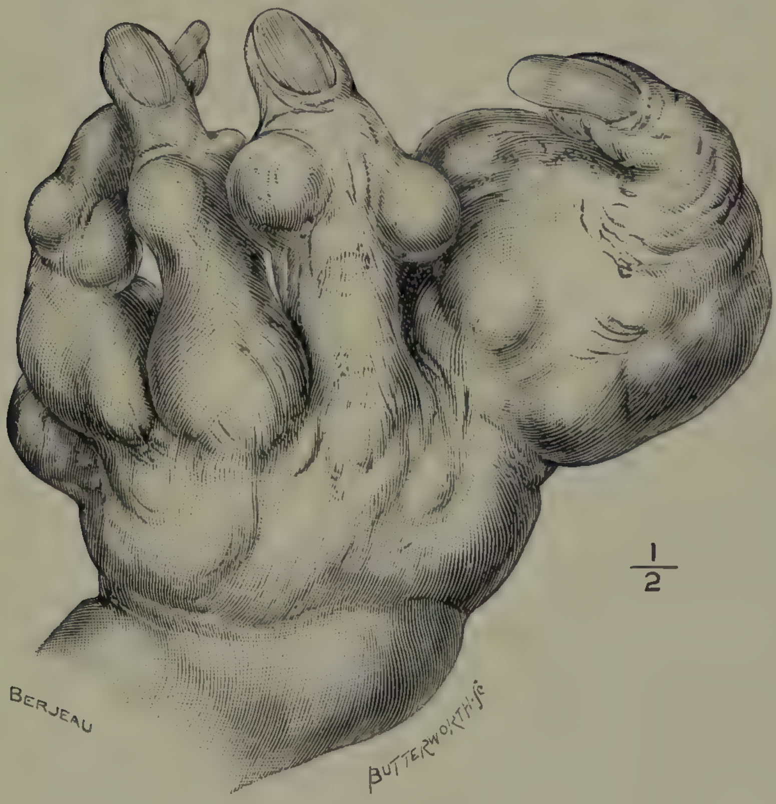


FIG. 188.—A HAND WITH MULTIPLE CHONDROMATA.

Chondromata are always encapsuled and form deep hollows in the bones from which they arise; they are painless, grow slowly, and are firm to the touch. Occasionally the cartilage softens from mucoid degeneration, and this softened area may give rise to a sense of fluctuation. This serves to distinguish them from osteomata, which they resemble clinically. Chondromata calcify in adults and sometimes ossify.

The Museum of St. George's Hospital contains a very remarkable chondroma which arose in the mesethmoid of a young woman, and filled the nasal fossæ, occupied the orbits, and dislocated the eyeballs outwards. It filled the antra, expanded the nasal bones, invaded the sphenomaxillary fossæ and formed a large mound in the anterior fossa of the skull, and almost reached the roof of the cranium. Its disruptive effects upon the facial bones were very extraordinary. In spite of this, the patient's health was but little disturbed; she had no loss of intellect and, it is believed, no paralysis. The course of the disease from the time the tumor was detected till the patient died was about six years.

Large chondromata of this kind are exceptional, and it is necessary to remember in connection with this case that the mesethmoid is a plate of hyaline cartilage at birth and continuous with the triangular or septal cartilage of the nose.

Large chondromata arise from the sacrum and the innominate bone, and when they grow from the inner aspect of this bone in women they may in some circumstances be indirectly fatal, as the following case demonstrates:

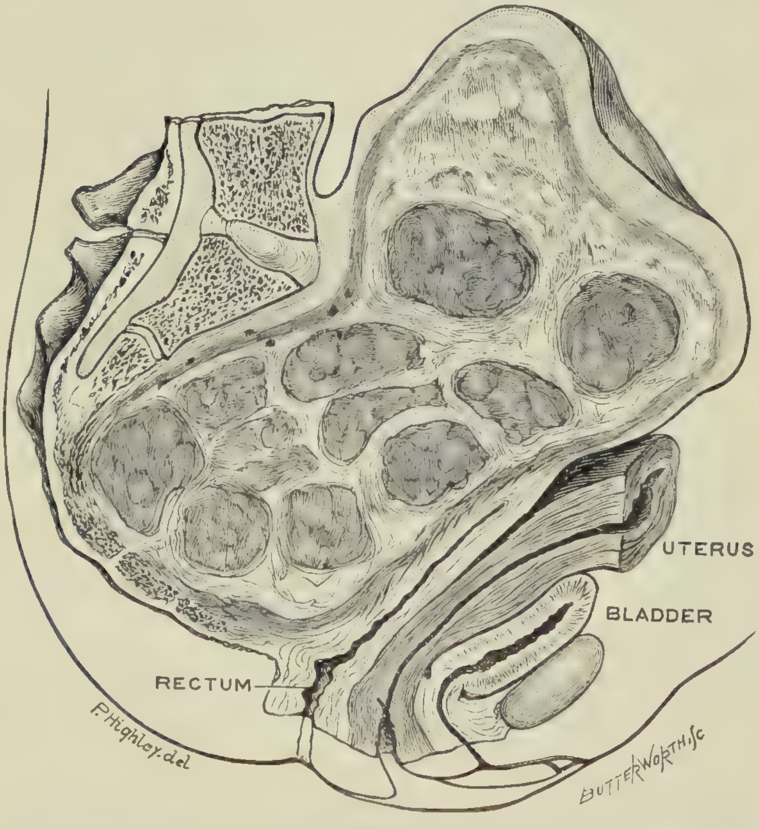


Fig. 189.—Pelvis in Section with a Large Chondroma Arising from the Sacrum and Obstructing Delivery at Term. The dark patches are spurious cavities due to softening. (From Bland-Sutton, "On Tumours.")

A woman aged twenty-one years was admitted into University College Hospital, London (1893), in labor, the transit of the fetus being obstructed by a solid tumor in the pelvis. Hysterectomy was promptly performed and the life of the child preserved. The mother died nine days after the operation. The parts concerned are shown in sagittal section in Fig. 189. The tumor, a partially ossified chondroma, has a firm fibrous capsule; the spaces in it are spurious cavities due to softening of its tissues. The tumor is intimately connected with the third, fourth, and fifth sacral vertebræ, and it has utilized all the available space in the true pelvis and has displaced and compressed the rectum, vagina, and urethra against the pubes. The ovoid shape of the tumor, and in consequence its elliptical outline, is characteristic of all tumors which mould themselves in the true pelvis—*e. g.*, the pelvic segments of large ovarian cysts and cervical fibroids and the head of the fetus after a long labor. The most lethal effect of the tumor, even more than the obstruction it offered to delivery, is the insidious change it produced on the ureters, for both were dilated, and the pelvis of each kidney contained pus. The presence of the tumor had been known seven years previous to her tragic death.

Chondromata arising from tracts of hyaline cartilage in the adult are very rare, and it is rarer for them to attain an important size. Small nodular outgrowths are met with along the margins of articular cartilages and those of the larynx, and the triangular cartilage of the nose: such are often termed ecchondroses. Those which grow from the larynx are the most important: they arise from the thyroid, cricoid, and occasionally the arytenoid cartilages. Small ecchondroses growing from the inner surfaces of the laryngeal cartilages are more dangerous than the larger examples springing from their outer surfaces. Ecchondroses, when projecting into the larynx, are covered with its mucous membrane; they may be smooth or tuberculated, round or conical. In exceptional cases the overlying mucous membrane has been found ulcerated. Chondromata, when they project into the larynx, produce stridor, difficulty in breathing, and sometimes interfere with the movements of the vocal chords. When the tumors only involve the outer surfaces of the laryngeal cartilages, they do not, as a rule, produce any inconvenience, unless they are exceptionally large.

Hyaline cartilage is found as a constituent in many tumors, *e. g.*, dermoids, sarcomata of the testis, breast, and particularly tumors of the parotid, lacrymal, and submaxillary glands. This anomaly will be discussed with the sarcomata.

Treatment.—The operative treatment of chondromata has been greatly simplified since surgeons have appreciated the fact that these tumors, when growing in relation with bones, are distinctly encapsuled. Now, when it is necessary to interfere with a chondroma, even in cases where several tumors are present, it has become customary to incise the capsule and shell out the cartilage. In most instances this simple method is successful. Exceptionally, however, cases come under observation which demand more serious measures. When the tumors are very numerous on the bones of the hand, the fingers are so crippled and useless that amputation has been performed. Fortunately, such severe treatment is very rarely needed.

Osteomata (Osseous or Bony Tumors).—An osteoma is a tumor composed of bone, and may be defined as an ossifying chondroma, for every growing osteoma has a cap of hyaline cartilage which has the same relation to its growth that an epiphysis bears to the growth of a long bone.

There are two species of osteomata, the compact and the cancellous.

Compact or hard osteomata are in structure identical with the compact tissue which forms the shaft of long bones. They are usually sessile and grow most commonly from the bones of the skull, especially in the neighborhood of the external auditory meatus, the orbits, and from the angle of the mandible. Many of the large and exceedingly hard tumors removed from the antrum and described as exostoses have been found after careful microscopic examination to be odontomes. The small hard osteomata which grow from the margins of the external auditory meatus have been especially studied because they obstruct this passage and cause deafness: it is not rare for them to be bilateral. Large osseous tumors of the facial bones sometimes produce hideous deformity and occasionally destroy the eyeball. The clinical history of some of these cases is very remarkable. Thus, a patient who came under the care of Lediard presented the condition shown in Fig. 190. This man, a sailor, thirty-three years of age, stated that the tumor was noticed at birth, and seemed scarcely larger than a pea; it slowly increased in size, and at the age of nine years destroyed the eyeball. When he was twenty-five years old, the skin of the eyelid sloughed. Eight years later the osteoma fell out of the orbit.

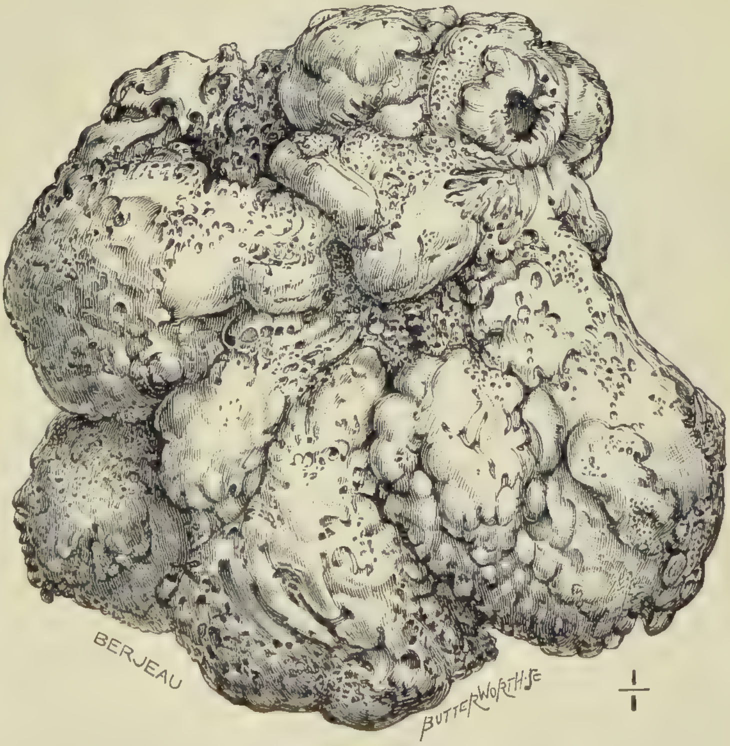


Fig. 190.—An Osteoma Weighing 9½ Ounces which Grew from the Orbit and was Detached Spontaneously. (Museum Royal College of Surgeons.)

The spontaneous detachment of osteomata in this way has been recorded by several observers and is due to necrosis of the tumor.

Cancellous or soft osteomata resemble in structure the cancellous tissue of bone, and are soft in comparison with the preceding species. They possess a thick covering of hyaline cartilage, and when growing at the distal end of the radius or tibia present a series of deep channels for the passage of tendons. Occasionally an osteoma is pedunculated; more frequently it has a broad base. Osteomata, whether sessile or stalked, usually grow slowly, but in the course of years they sometimes attain large proportions. They are innocent tumors, but occasionally imperil life by mechanically interfering with the function of vital organs. Reid described a case in which an osteoma grew from the posterior surface of the odontoid process and projected into the neural canal to the extent of 8 mm. and compressed the spinal cord with fatal effect. Although in themselves painless, osteomata often induce pain by pressing on nerve trunks in their vicinity.

Large osteomata occasionally arise from the pelvic aspect of the innominate bone, and in certain circumstances have constituted an effectual bar to delivery of the fetus at term. All complete works on midwifery describe examples.

Cartilage-clad osteomata occasionally occur in multiples on the humerus, radius, ulna, femur, tibia, and fibula; they are often congenital, occasionally hereditary, and frequently exhibit bilateral symmetry in so far as position is concerned.

In clinical and pathologic writings care should be taken to distinguish between abnormal formations of bone, such as ossification of tendons, calcification of inflammatory exudations, and the like.

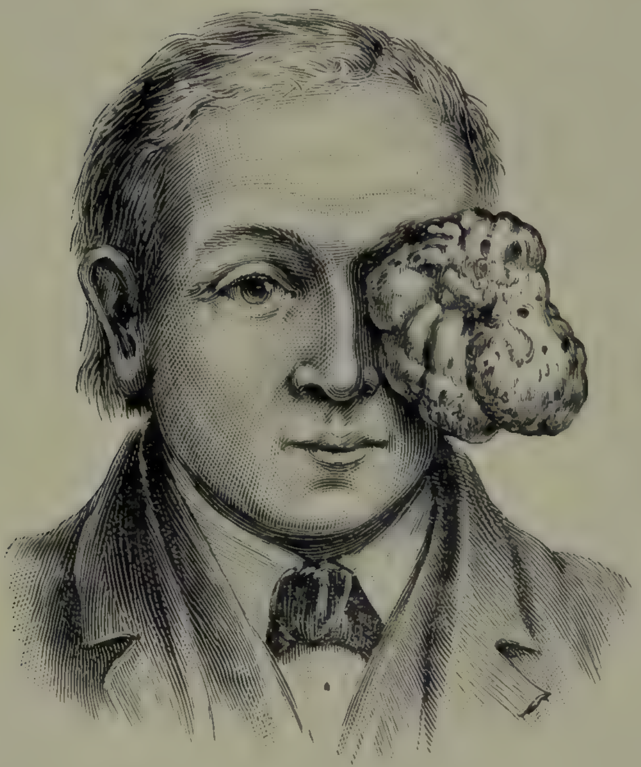


FIG. 191.—THE APPEARANCE OF THE SAILOR WITH THE TUMOR IN POSITION. (From a water-color sketch in the Museum of the Royal College of Surgeons.)

In the early writings on tumors all abnormal formations of bone which bore the least resemblance to a tumor were termed exostoses, but the term is sharply limited now to outgrowths of bone at the points of insertion of powerful muscles. The long bones of a child at birth are smooth in outline and almost cylindrical in shape; the periosteum is relatively thick, and gives attachment to the muscles. On examining the long bones of an adult muscular man, their shafts are found to be irregular, and present many asperities, such as the linea aspera, gluteal ridge (sometimes called the third trochanter), oblique lines, and the like. These ridges and lines, in the majority of instances, are the ossified insertions of muscles, and occasionally they are so pronounced as to be appreciable through the soft structures, and are then described clinically as exostoses. The two most frequent examples of this form of exostosis are the adductor tubercle of the femur and the tubercle on the first rib at the insertion of the scalenus anticus. Probably the most common exostosis is that which occurs in the tendon of insertion of the abductor magnus: it usually assumes the form of a broad ledge of bone; exceptionally it is stalked, and in rare cases surmounted by a bursa; the walls of such bursæ are now and then furnished with villi, and even loose bodies have been found in them (Orlow). Care must be taken not to confound a supracondyloid process of the humerus, and the occasional third trochanter of the femur, with exostoses.

Clinical Characters.—Osteomata are easily recognized on account of their extreme hardness and in being localized to bones; they rarely cause pain except when growing in the vicinity of, and pressing upon, the trunks of nerves. Osteomata near the external auditory meatus will occasionally interfere with hearing, and if bilateral and they completely block both meatuses will cause total deafness. A large osteoma of the frontal sinus and orbit will sometimes seriously distort and dislocate the eyeball, as well as produce hideous deformity. In determining the character of osteomata of the limb bones, the X-rays render very valuable assistance, especially in regard to their attachments.

Treatment.—Osteomata, unless they interfere with nerves or the movement of joints, or in the case of the facial bone produce deformity or deafness, are rarely interfered with. In a case of large pelvic osteoma under my care, a rounded process of the tumor pressed upon the great sciatic nerve as it issued from the pelvis. This offending process was exposed through an incision in the buttock and detached with chisel and mallet. Pedunculated osteomata may be easily removed with stout forceps. Sessile osteomata of the ivory variety sometimes require the most persevering efforts of the surgeon, aided by the best surgical cutlery. When exostoses are seated near joints and the synovial membrane is likely to be opened in the operation, they should not be removed unless they produce grave interference. It should always be remembered that in removing osteomata and exostoses the cancellous tissue of the bone from which they grow is opened.

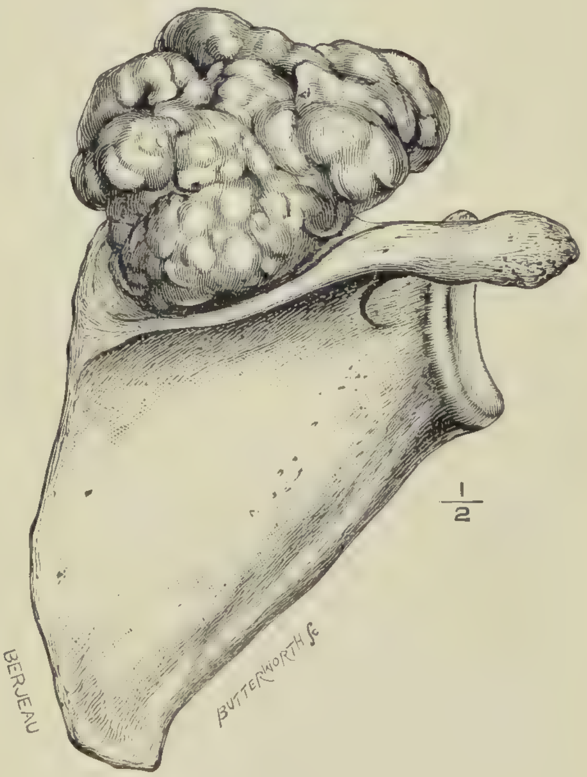


FIG. 192.—OSTEOMA OF THE SCAPULA. (Museum Royal College of Surgeons.)

Cranial osteomata are, as a rule, formidable objects; when growing from the roof of an orbit, or frontal bone, they not infrequently extend as deeply into the cranial cavity as they project beyond it.

Myelomata (Red-marrow Tumor).—A myeloma is composed of tissue identical with the red marrow of young bone.

These tumors were formerly classed among sarcomata (myeloid sarcoma), but they differ from them in many points, and above all in the fact that they are not malignant. They arise only in the cancellous tissue of bone. When fresh, the cut surface of the tumor is deep red, and looks not unlike a piece of fresh liver, and is very vascular. Microscopically this tissue abounds in large multinuclear cells (giant cells, myeloplaques) embedded among round and spindle cells. The giant cells are so numerous as to constitute the greater proportion of the tumor.

The distribution of myelomata is that of red marrow, but they exhibit a striking preference for certain bones. The tibia is the favorite bone in the lower, and the radius in the upper limb; while so far as the bones of the head are concerned myelomata seem peculiar to the jaws, and they are apparently unknown in the vertebræ. In regard to the jaws they occur in the body of the mandible and the alveolar border of the maxilla. I have had two cases in which a myeloma arose in and was confined to the premaxillæ. These tumors occur in the clavicle and select the sternal end of this bone, but in one case recorded by me the acromial end was attacked. In the humerus the head is preferred; in the femur, the condyloid end, and a myeloma has been observed in the patella.

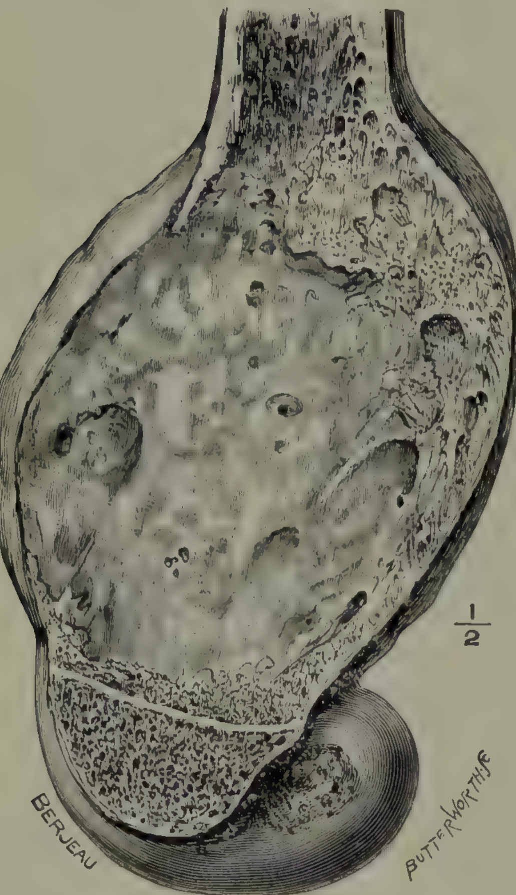


FIG. 193.—LOWER END OF THE FEMUR IN SECTION TO SHOW A MYELOMA.

From a girl aged seventeen years: she was known to be alive and well five years after amputation through the middle of the thigh.

Clinical Characters and Treatment.—Myelomata are rare tumors after the age of twenty-five years; they grow slowly and very gradually expand the bone immediately investing them, which occasionally becomes so thin as to crackle on pressure. The soft tissue of the tumor sometimes perforates its bony capsule and pulsates synchronously with the beat of the heart. Myelomata do not infect lymph glands or undergo deportation (dissemination), and if removed before the tumor-tissue perforates the capsule they do not recur. This fact is important in regard to treatment, for instead of amputating limbs to cure them, surgeons now excise the affected section of the bone whenever this is possible and leave the patient a useful limb. Successful treatment of this kind has been carried out in connection with the ulna, radius, humerus, clavicle and even in connection with the tibia.

Paget proved that myelomata may be scraped out of their capsules, and his example has been followed in many instances with success. It is fair to assume that the tumor Mott excised with the sternal two-thirds of the clavicle for what he called in the terms of his day (1827) "an osteosarcoma" in a lad aged eighteen years, was in all probability a myeloma. The patient survived the operation fifty years.

Fibromata.—Fibromata, or tumors composed of fibrous tissue, were formerly supposed to be very common, but careful histologic research has shown that tumors consisting almost entirely of fibrous tissues are rare. For instance, it was the fashion to describe as fibromata those tumors of the uterus now known as myomata and fibromyomata; traces of this belief linger still in the term "uterine fibroids." Many tumors now recognized as spindle-celled sarcomata were a few years ago named "recurring fibroids." The difficulty of distinguishing between a myoma, a slowly growing spindle-celled sarcoma, and a pure fibroma is well known to skilled histologists.

A tumor with the structure of a fibroma growing on the gums was called an epulis, but the term never had more than a topographic significance. When such a tumor grew on a nerve, it was termed a neuroma. Fibroids of the uterus are of such significance that they demand separate consideration (p. 771). Ovarian fibroids have recently been extricated from the spindle-cell sarcomata.

Sarcomata.—Without any extravagance a sarcoma may be regarded as a malignant tumor-disease of connective tissue. It may arise in any situation where connective tissue exists. Sarcomatous tissue also gives rise to some of the more complicated varieties of connective tissue, such as hyaline cartilage, bone, and a peculiar variety of cell known as the striated muscle spindle.

It is very necessary in studying the distribution of sarcomata among complex organs to remember in discussing the pathology of this disease that a sarcoma of a kidney, or of the intestine, the mammary or prostate gland rarely arises in the gland itself but usually in the connective tissue which forms its capsule, and subsequently invades the true tissue of the organ.

We will briefly consider the histologic details of the various species of sarcoma and then consider the way in which they betray their malignity.

Sarcomata are named according to the prevailing type of cell composing them. *Round-cell sarcomata* consist almost entirely of round cells, each possessing a large round nucleus, which is always conspicuous in stained sections. The cells of the tumors are separated from each other by delicate intracellular substance: blood-vessels are abundant, but lymphatics are absent.

The round-cell sarcoma is the most generalized tumor that affects human beings; it occurs in bone, muscle, nerves, glandular and muscular organs, ovary, testis, thymus, adrenal, and even in the delicate tissue of the retina; it may arise at any period of life, even in the unborn.

One variety of the round-cell sarcoma reproduces the delicate structure of a lymph gland and is termed in consequence *lymphosarcoma*. It arises in situations where lymphoid tissue abounds, *e. g.*, the tonsil, base of tongue, mediastinum, and the retroperitoneal tissue.

Spindle-cell sarcomata are composed of cells resembling spindles, and though the cells of a tumor often display extraordinary uniformity, there is great diversity in the size of the cells in different tumors. In some the cells are small and oat-shaped, others are fusiform; often they may be attenuated, and in other tumors large and plump. In some situations, especially the shafts of long bones, spindle-cell tumors contain tracts of hyaline cartilage; these are called chondrifying sarcomata, and the cartilage may be so abundant as to constitute the bulk of the tumor. This cartilage is sometimes calcified. Such tumors are sometimes called "malignant enchondromata." There is an important clinical distinction between such tumors and benign chondromata, for the latter are congenital or arise in early childhood.

The most remarkable feature found in these tumors is the presence of spindles with transverse striations like those which exist in young (embryonic) muscle cells. Tumors which contain transversely striated spindles are known as myosarcomata, and they occur in the most unexpected situations, such as the testis, sinus of the kidney, and neck of the uterus, where striped muscle tissue is not found normally.

One of the most striking species of sarcomata is that to which the adjective melanotic is applied on account of its blackness. (See Pigmented Tumors, p. 753.)

Sarcomata are distinguished from the chief genera of connective-tissue tumors in that they rarely possess capsules, and when they do it is generally a spurious encapsulation depending on environment, such as when they arise in the eyeball, in the medullary cavity of a long bone, or in the sinus of a kidney. Having no restraining capsule they infiltrate adjacent tissues, and this is particularly dangerous when a sarcoma arises in the midst of important structures. Thus, in the mediastinum an infiltrating tumor may involve the esophagus, trachea, lung, vagus nerve, pleura, pericardium, vena cava, and even the aorta.

A sarcoma of the kidney will creep into the renal vein and invade the inferior vena cava; a sarcoma of the thyroid gland will implicate the trachea, recurrent laryngeal nerve, and the jugular vein. This infiltrating propensity of sarcomata, apart from its effects on neighboring organs, has an important bearing on treatment. When the surgeon attempts to remove a sarcoma effectually, it is of the utmost importance to cut well wide of it, for if small portions of the tumor are left behind the sarcoma grows again from these remnants (recurrence).

The vascularity of sarcomata varies. In all the circulation is mainly capillary; the very soft, quickly growing, round-cell species are often so abundantly supplied with arterial blood that they pulsate. This movement is sometimes obvious to the eye as well as the hand. The circulation through the tumor often produces a murmur or hum. These are clinical signs of great value in differential diagnosis.

The intimate relation of sarcomata to blood-vessels has an important relation to the distribution of their cell-elements to other parts of the body: for example, the cells from the tumor find their way to the venules which return the blood into the large veins and are conveyed as minute emboli to the lungs; these cells are arrested in the pulmonary capillaries and they behave as grafts, retain their vitality and form what are known as secondary nodules or deposits. There is no limit to the number of these secondary deposits, and a hundred or more may sometimes be counted in the lungs. When the primary tumor is situated in a part from which the venous blood enters the portal circulation, the emigrant cells from the tumor are received by the capillaries of the liver and secondary nodules grow in this organ. This remarkable phenomenon known as dissemination is one of the most dangerous features displayed by sarcomata.

Although sarcomata as a genus are ubiquitous, nevertheless they occur in some situations more frequently than in others and present some striking age-relations as well as peculiarities in distribution which are worthy careful study. Take, for example, the eyeball: this sense-organ is liable to two very distinct species of sarcoma. During infancy sarcomata arise in the retina and possess the minute structure of its sustentacular framework as it exists in the embryo. These tumors often arise in both retinæ, and though they rarely disseminate are extremely prone to recur in the stump of the optic nerve after removal of the globe. Adults are also liable to sarcomata in the eyeball, but they arise in the uveal tract, and contain pigment. This species of sarcoma is invariably unilateral, and though not so liable to recur locally, is dreadfully prone to disseminate, and in some cases infects almost every organ in the body.

The kidneys, ovaries, and adrenals are liable to become the seat of sarcoma in infancy, and in a fair proportion of instances the disease is bilateral. Sarcoma of these organs in adults is invariably unilateral.

Sarcomata occur more frequently in the structures of the lower than in those of the upper limbs. This is true of the bones, muscles, and nerves. Sarcomata are common in the bones, especially the long bones of the limbs; they may arise in the shaft of the bone, and are then termed central sarcomata; more frequently they grow in connection with the osteogenetic layer of the periosteum—periosteal sarcomata—and sometimes attain huge proportions.

Sarcomata attack the scapula and innominate bones in about equal proportions; they arise in the femur more frequently than in the humerus, but they are deadly tumors in both situations, especially when growing from the trunk-ends of these bones. Sarcomata rarely attack the radius and ulna; they are comparatively rare in the fibula, but common in the tibia. Although there are no microscopic distinctions in the sarcomata arising in the tibia from those which grow in the femur, nevertheless the tibial tumors are far less malignant and recurrence after amputation is often long delayed.

In the case of sarcomata arising in nerves, the great sciatic or its branches, the popliteal, posterior tibial, or peroneal nerves are attacked. In connection with muscle, although primary sarcomata have been observed in the pectoralis major, triceps, and rectus abdominis, the greater number of examples have occurred in the lower limb and include the gracilis, tensor vaginæ femoris, peroneus longus, sartorius, and tibialis anticus. Two precautions are necessary in considering the question of primary sarcoma of a muscle, for it is a rare occurrence; in the first place, avoid mistaking a gumma for a sarcoma, and in the second remember that periosteal sarcomata are extremely prone to infiltrate the sheaths of adjacent muscles.

Unfortunately there is only one way of effectively treating sarcomata of long bones, nerves, and muscles of the limbs, and that is by amputation.

The greater liability of the lower limb as compared with the upper to be the seat of sarcoma is further borne out by a study of primary sarcoma of synovial membrane: nearly all the recorded examples of this rare disease arose in the synovial membrane of the knee-joint; in this form of sarcoma, although success has followed erasion and excision of the joint, amputation has proved the best safeguard against recurrence.

Chondrifying Tumors of the Salivary Glands.—These extraordinary tumors are a great puzzle to systematic writers. It is usual to place them among sarcomata because they contain hyaline cartilage, but epithelial elements are very abundant in them. Some writers, especially Nasse, regard them as endotheliomata (see p. 770). Other writers, equally puzzled by the complexity of the tissues, describe them as "mixed-tumors." For the present they may remain among the sarcomata. It is curious that no example of this kind of tumor has been found in the pancreas.

Chondrifying Tumors of the Parotid Gland.—These appear as oval, smooth, and elastic swellings in the parotid immediately in front of, or behind, the angle of the mandible; increasing in size, they become tuberous and may implicate the tragus. Left to themselves, they burrow deeply among the tissues of the neck, dip beneath the sternomastoid, and acquire attachments to the carotid sheath; sometimes they creep upwards and adhere to the under surface of the petrosal, and, pushing towards the middle line, so bulge the pharyngeal wall inwards as to impede deglutition. Rapidly growing tumors tend to involve the skin and ulcerate; in very large tumors semifluctuating spaces form in consequence of degenerate (mucoid) changes.

The facial nerve is usually involved in large parotid tumors; the small specimens which burrow behind the ramus of the mandible often implicate the nerve as it issues from the stylomastoid foramen.

Structurally, these tumors exhibit extraordinary variety. Some consist entirely of hyaline cartilage arranged in lobules bound together by loose connective tissue. The cells of the cartilage rarely possess capsules, and are often stellate, as in immature cartilage. Such grow with extreme slowness, and rarely exceed a bantam's egg in size, and may require ten or even twelve years to attain such proportions.

The large, rapidly growing tumors consist of spindle cells in which tracts and islets of hyaline cartilage are interspersed. When chondral tissue is abundant, it is very prone to mucoid changes, and soft, fluctuating spaces are formed. The connective tissue is very liable to undergo myxomatous change, and, as if to render these tumors more complex, portions of the secreting tissue of the gland are imprisoned in them.

It is not unusual in sections from a parotid sarcoma to meet with spindle cells, cartilage, myxomatous tissue, glandular acini, and fibrous tissue in an area of 2 cm. square. Exceptionally, transversely striped spindle cells are seen. Parotid tumors of such complex structure grow rapidly, and attain a large size, and often infiltrate the surrounding tissue and skin. Some of them infect the adjacent lymph glands and give rise to secondary deposits in the lungs.

Chondrifying sarcomata of the parotid are most frequently met with between the fifteenth and thirty-fifth years, but they have been observed as late as the seventy-fourth year. They present very characteristic features. In their early stages they are easily removed, but many of the rapidly growing forms so quickly infiltrate the tissues that their complete extirpation is not always possible.

When left to themselves they cause death in a variety of ways. Thus, they may press upon the pharynx and lead to fatal dysphagia, or ulceration may open some large vessel in the neck and produce fatal hemorrhage; secondary nodules sometimes form in the lungs, and induce fatal bronchopneumonia, but dissemination is not a common feature of sarcomata of the salivary glands.

These tumors are far less frequent in the submaxillary than in the parotid gland. They are encapsuled and, as a rule, shell out easily. They grow slowly, and occur in the young as well as in adults. Glandular tissue is often associated with the cartilage.

The most remarkable features of sarcomata of the salivary glands, and of the parotid in particular, are these:

An individual may have a tumor in one of these glands which will grow to a certain size and be stationary for ten, fifteen, and even forty years; then without any warning it begins to enlarge and infiltrate the gland, cause pain, and disseminate, and destroys life in a few months. In another class of case the tumor will make its appearance, grow quickly, ulcerate, and destroy the patient in six or nine months; the microscopic structure of the tumors in both cases being similar.

Chondrifying Tumors of the Lacrymal Gland.—This gland is occasionally the seat of this variety of tumor, and their histologic and clinical features are identical with those arising in the parotid.

Adenoma of the Palate.—The tumors to which this name is applied are very rare; they are oval or globular in shape and vary in size from a cobnut to a ripe fig, and are more often lodged in the soft than the hard palate and possess perfect capsules from which they are easily enucleated in the course of an operation. Their structure is very complex: some possess glandular tissue with ducts and acini embedded in a stroma resembling sarcomatous tissue. Epithelial pearls are abundant, some of which may be keratinized. Myxomatous tissue may be present and lymphoid follicles. These tumors may occur at puberty, but are more common between the thirtieth and fiftieth years. They are benign.

These tumors have greatly puzzled taxonomists. Some writers place them with dermoids, others among the teratoid tumors, and many class them with the "mixed tumors" of the salivary glands.

Pigment-containing Tumors.—Under this heading will be considered the tumors known as melanomata on account of the black pigment they contain, and which are usually classed in the genus sarcomata. Some of them are undoubted carcinomata, hence it will be convenient to discuss them together.

Among other pigment changes associated with morbid growths it is necessary to mention the rare affection chloroma (green cancer) and a peculiar bronzing of the skin arising in children with sarcoma of the adrenals; the small multiple red nodules of the skin known as De Morgan's spots (see p. 804) and a peculiar red coloration often seen in degenerating fibroids of the uterus, especially when complicating pregnancy; the curious colored patches of the skin known as freckles and the larger and more prominent patches common about the eyelids, and termed in consequence xanthelasma palpebrarum. The remarkable abnormal pigmentation of cartilage known as *ochronosis* is not associated with tumors, but with a rare anomaly of the urine termed *alkaptonuria*.

Melanosis and Melanomata.—In the majority of mammals there are certain epithelial and connective tissues which normally contain pigment. Among pigmented tissues the skin and epithelial layer of the retina hold the first place. In the skin the pigment is chiefly contained in the deeper layers of the rete mucosum; hair, being derived from the cells of this layer, is pigmented also. In many mammals other tissues contain pigment, such as the mucous membrane of the roof of the mouth of the dog, and the blue coloration of the vaginal mucous membrane of the vervet monkey.

In man the amount of pigment in the skin varies greatly, so that we may pass gradually from individuals whose skins are intensely black to others who have no trace of cutaneous pigment.

It is a noteworthy fact that animals with no pigment in the skin also lack pigment in the uveal tract of the eyeball. A familiar example of this is the white rabbit with pink eyes. Such a condition is termed *albinism*, and colorless animals, or *albinos*, occur among all classes of animals, vertebrate and invertebrate. Excessive development of black pigment in the skin is known as *melanism;* this is much rarer than albinism.

Abnormal distribution of pigment is common; in man it gives rise to the condition termed leukoderma when it affects the skin, and unequal distribution of pigment in the retina is known as retinitis pigmentosa. Irregular patches of black in the skins of horses cause them to be described as piebald, and when disseminated in small dots and irregular tracts they are said to be gray.

In the white races of men the pigment granules are almost entirely confined to the cells of the rete mucosum, but when the pigmentation is very marked it will be found distributed in the other tissues of the skin. The pigment, or melanin, as it is called, lies within the cells either in the form of black or brown granules, or they may be uniformly stained by it. It is stated that white skin transplanted on to a negro soon becomes pigmented, and that the skin of a negro grafted on to a white man undergoes depigmentation. It has long been known that leukocytes carry pigment.

In amphibians and fishes pigment occurs in the branching cells (Deiters' cells) situated beneath the epidermis. These cells are filled with black melanin granules, obscuring the nucleus. On exposure to light these protoplasmic processes retract, and the pigment is concentrated in the cell body, but when kept in the dark the processes are protruded and the pigment is diffused in the surrounding structures.

The most remarkable example of pigment formation is found in the cuttle-fishes (*Octopus* and *Sepia*). These invertebrates possess an ink-bag from which when irritated they eject a black pigment (sepia) in such abundance as to color the surrounding water to the extent of a cubic yard or more, and under cover of this dark cloud escape from their enemies.

Pathologic pigmentation in its most serious form is found in connection with certain tumors arising in the skin or within the eyeball; the color being due to the presence of a black pigment known as melanin, the tumors are in consequence termed melanomata. The amount of melanin in these tumors varies greatly: in some the quantity is so small that the tissue presents merely a brown coloration, while in others it is so abundant as to make them as black as ink. The pigment particles are lodged not only in and among the characteristic cells of the tumors, but in and among those of its fibrous matrix, even in the walls of its blood-vessels. The primary tumor may contain very slight traces of pigment, sometimes so slight as even to raise a doubt whether it should be called melanotic; yet the secondary growths and the lymph glands infected by it will be of an inky-black color. The intense blackness of the secondary deposits leads to their ready recognition, and doubtless accounts for the belief that this species becomes more widely disseminated than other malignant tumors; but an equally wide distribution of secondary nodules in unpigmented tumors will sometimes be found when the organs are submitted to a rigorous search.

Exceptionally the secondary deposits from a melanoma may contain so little pigment as to appear colorless to the naked eye.

Melanin.—This is a pathologic pigment and can only be formed by the action of living protoplasm; when seen in mass it is black, but by transmitted light resembles sepia. It is soluble in ether, alkalies, and strong acids, and is bleached by chlorin, a fact which is useful in examining the microscopic features of melanomata.

The urine of patients with melanotic tumors often contains black pigment (melanogen), usually in solution, but occasionally suspended in the form of granules. The urine is, as a rule, clear when first voided, but blackens on exposure to the air and becomes intensely black when submitted to oxidizing reagents, *e. g.*, a mixture of sulphuric and hydrochloric acids to which a few drops of ferric chlorid have been added.

A more sensitive test is the addition of bromin water to the urine, which yields a yellow precipitate, turning black on exposure to light. I made several observations on the urine of patients suffering from melanomata in the hope that some opinion might be formed as to the gravity of the patient's condition according to the amount of melanin present. In two cases the patients died within three months of the observation, although the urine was free from black pigment, but, on the whole, I am inclined to believe that an abundance of melanin is of the gravest import.

Primary Melanomata of the Skin.—These tumors arise in the skin in several ways; the common source is pigmented moles and warts. Rarer examples of the disease arise in the fingers and toes, especially in the pigmented patches sometimes found near the matrix of the nails (melanotic whitlows). Another source is the dark skin of the external genital organs in both sexes and that around the anus. Melanotic tumors may also arise independently of birth marks on any other pigment anomaly of the skin. I have seen two instances in which the disease arose in the skin under the heel, following in each instance an injury from a nail in the boot. The disease in these patients ran a rapidly fatal course.

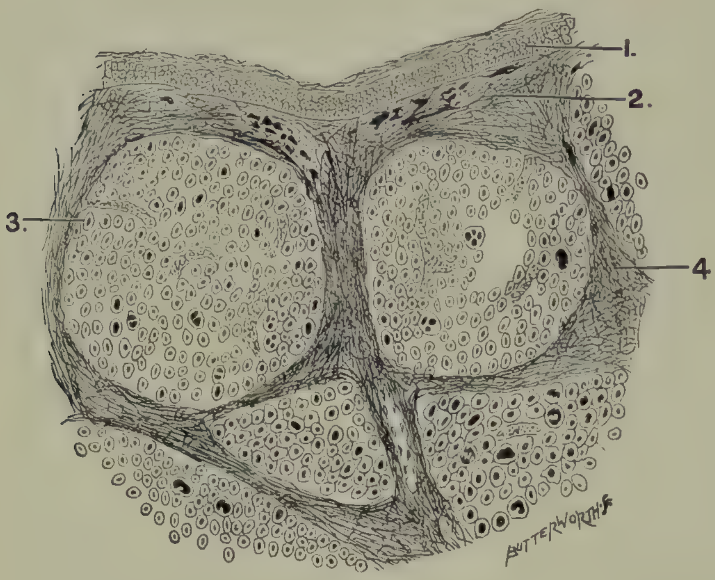


Fig. 194.—Microscopic Characters of a Melanoma Arising in a Mole (Acton).

1, Epidermis; 2, corium with Deiters' cells; 3, alveolar spaces with cells; 4, interalveolar stroma.

As pigmented moles and warts are the common source of primary cutaneous melanomata it will be necessary to consider these defects of the skin.

Moles.—These are pigmented and usually hairy patches growing on the skin (*nævus pilosus*). They are congenital or appear during infancy. The patches vary in size: many are no larger than a split pea; others are as big as the palm, and in some instances cover an extensive area of the trunk, face, or limbs. Fifty or more moles may be present on an individual.

The color varies; in some it is brown or of a coffee-color, others are as black as ink. The hair on a mole may be short, like that on the body generally, or as long as that on the scalp. Some black blemishes are glabrous (nævus spilus).

The most striking feature in the histology of a mole is the alveolar arrangement of the tissue immediately underlying it. The nerves in the subcutaneous tissue beneath a large mole often exhibit the condition known as a plexiform neuroma (see p. 764).

Melanomata arise quite as frequently from a black hairless blemish (nævus spilus) as from the hairy nævus; another source is the pigmented wart or congenital papilloma. This kind of wart appears in two forms: the most frequent is the large solitary wart which stands up on the skin, usually of the trunk, like a mulberry with a stalk. This variety of wart is either congenital or appears in childhood; it is always solitary and contains black pigment. After middle life it may become active, ulcerate, stink, and in a certain proportion of the patients, infect the system with melanomatous nodules.

The rarer form consists of an area composed of a number—twenty or more—of flat-topped, closely set, sessile, soft warts. These may be intensely black. Without any obvious reason this wart-field increases in size, infects the glands, and melanin appears in the urine. A striking case of this came under my care in a girl aged fifteen years; it is the earliest age at which I have seen a melanoma. The primary tumor was seated on the skin covering the left mamma.

A pigmented mole may remain quiescent throughout a very long life and never cause the least inconvenience; in other instances, as life advances the mole ulcerates, perhaps bleeds freely, and may even become partially healed; but coincident with the onset of ulceration the adjacent lymph glands enlarge, become charged with pigment and cystic spaces filled with inky fluid form in them, and finally the overlying skin ulcerates. The infection may not proceed further than this; recurrent hemorrhages from the fungating glands or a furious bleeding, should a large vein or artery become broached by ulceration, carries off the patient. In many cases the morbid material is disseminated into distant parts, secondary knots form in the liver, lung, kidney, or brain, and death arises from interference with the functions of these organs.

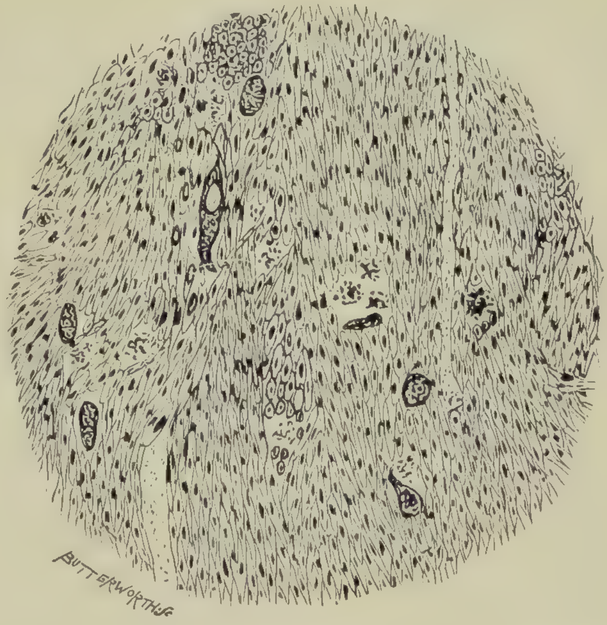


FIG. 195.—MICROSCOPIC APPEARANCE OF A MELANOSARCOMA (after Acton).

In other cases the mole, instead of ulcerating, is observed to become more prominent, and finally forms a tumor of some size standing out prominently from the skin. In due course the lymph glands, in anatomic relation with the part from which the tumor arose, enlarge, and secondary deposits occur in the viscera, bones, or skin.

It does not necessarily follow that in all cases of melanomata occurring in moles secondary deposits are formed in the viscera. In some cases, which, however, are very rare, the tumor seems to become mainly a source of pigment, large quantities of which enter the circulation, to be discharged with the urine, in which it is recognized as melanin. Exceptionally the skin will assume a dusky tint.

The hairy mole (dermoid pterygium) which occasionally grows on the conjunctiva is not, as far as my observations extend, liable to become the seat of melanoma.

Melanosis in connection with the *fingers* and *toes* assumes two forms: it may occur as a deep pigmentation of the skin, usually in the immediate neighborhood of the nail, often involving the matrix, and even the nail itself; or a small pigmented nodule will arise in the nail matrix or in the adjacent skin. These nodules quickly ulcerate, and dissemination follows.

Apart from abnormal deposits of pigment, such as moles and warts, melanomata are occasionally found in those parts of the body where the skin is more deeply pigmented than usual, namely, the external genitals in both sexes and the skin around the anus.

The greater *labia* are liable to melanosarcoma, and I have seen two examples: in each the disease ran the usual course. In one instance I have observed a spindle-celled melanoma of the *anus* in a woman of fifty years. Payr has recorded an example of a melanoma of the penis.

Primary melanoma of *mucous membrane* is very rare, and it is odd that the recorded cases have been observed on the mucoperiosteum of the hard palate. Treves, in recording an example, reminds us of the fact that the mucous membrane in this situation is charged with pigment in certain mammals. This is the case with dogs.

Intra-ocular Melanomata.—The commonest situation of these tumors is the uveal tract, and the seat of origin accounts for the presence of pigment. Their distribution in this tract is curious, for a melanoma of the choroid is ten times more common than in the ciliary body, and a pigmented tumor of the iris is excessively rare: moreover those which arise in the ciliary body are carcinomata.

Melanomata of the uveal tract are most frequent between the fortieth and sixtieth years, but they have been observed as early as the fifteenth and as late as the eighty-fourth year.

In structure they may be round-celled, spindle-celled, or mixed-celled, the size of the cells varying greatly in different tumors. The amount of pigment in intra-ocular melanomata varies greatly: in some specimens it is so abundant that the tumor is coal-black; in others it is only sufficient to impart a gray tint. Occasionally the pigment is so irregularly distributed that some parts of it are colorless.

The tumor remains for a time restricted to the interior of the globe, but it tends to escape therefrom in three directions: (*a*) along the course of the venæ vorticosæ, appearing outside the sclerotic in the situations where these veins emerge; (*b*) the presence of the tumor leads to an increase in the intra-ocular tension, and finally to sloughing of the cornea; (*c*) the growth may invade the optic nerve.

Melanosarcomata are very apt to recur after removal, and to become disseminated. The most frequent situation in which to find secondary deposits is the liver; but any organ may contain them, even the bones. It is surprising, considering that the eyeball is near to and in such close relation with the brain, by so large a nerve-trunk as the optic nerve, that it should be rarely implicated. It is a fact that when the brain is a seat of deposit it is rarely the result of extension along the nerve. The amount of dissemination varies greatly; in some cases secondary knots occur in almost every organ; in others they will be limited to the liver. The lymph glands adjacent to the orbit are rarely infected. It is curious that in most cases death results more often from the secondary growths involving important organs than from the local effects of the primary tumor. A rare complication of melanotic tumors is pigmentation of the skin.

The *duration of life* in patients with intra-ocular melanomata rarely extends beyond three years. A careful analysis of a large number of cases shows, however, that in many instances life may be indefinitely prolonged by early removal of the globe, and cases are known in which patients have been reported alive and well, five, six, eight, nine, sixteen, and eighteen years after the operation. In the majority of cases that recur the recurrence takes place within three years of the operation. Collins and Lawford, calculating cases in which recurrence does not take place within three years of operation as recoveries, come to the conclusion, from an analysis of seventy-nine cases of which they were able to obtain complete records, that the rate of recovery is twenty-five per cent., but they point out that patients have died from recurrence or secondary deposits after a much longer interval than three years. Dissemination has been deferred for so long a period as eleven years after excision of the eyeball (Hutchinson).

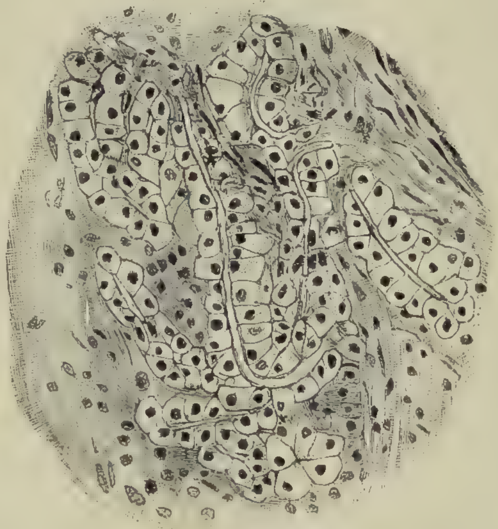


FIG. 196.—BLEACHED SECTION OF THE GLAND OF THE CILIARY BODY (after Treacher Collins.)

Melanocarcinomata.—Several writers who have devoted attention to intra-ocular tumors describe some of the pigmented tumors as carcinomata, using the term in the definite sense in which it is employed in this work. Much new light has been thrown on this question by the interesting investigations of Treacher Collins. This ophthalmologist has demonstrated the existence in the ciliary body, in the space extending from the root of the iris to the ora serrata, of a number of small tubular processes composed of epithelial cells with the free ends projecting towards the ciliary muscle. Collins succeeded in demonstrating the existence of these processes by bleaching the cells; he regards them as glands which secrete the aqueous humor. The ciliary glands are interesting in connection with melanocarcinoma, for Collins discovered among the intra-ocular tumors preserved in the museum of the Moorfields Hospital two examples from the ciliary body which were epithelial in character. In examining them he adopted the bleaching method to which reference has already been made.

We must agree with his observation that melanocarcinoma is unknown except as a primary tumor arising in the ciliary body.

Melanosarcomata in horses are of fairly common occurrence; the regions most affected are the tail and the parts about the anus, where they form large mushroom-like excrescences, with little disposition to ulcerate. The tumors in some cases attain large proportions, and have been known to weigh forty, fifty, and even sixty pounds. When a large tumor grows from a horse's tail it becomes a great encumbrance, which the veterinarian removes by amputation. It occasionally happens that in the operation a portion of the tumor is left behind, and its cut surface heals like other tissues. These pigmented tumors are very prone to disseminate, and secondary nodules occur in almost all the viscera; yet, in spite of this, melanosarcoma does not appear to be such a malignant affection in horses as in men.

Although most common in gray, it also occurs in white, and occasionally in black horses, and it certainly occurs in cows. Next to the anus and tail, the udder is the most frequent seat of the primary tumor, and it may spring up in the subcutaneous connective tissue in any part of the trunk. Horses may be attacked at any age from four years upwards. In structure melanosarcoma of the horse resembles a hard uterine myoma rather than a sarcoma. In these animals melanosarcoma of the uveal tract is very rare.

Sarcoma Idiopathicum Multiplex Hæmorrhagicum.—This rare disease, described by Kaposi, has been most frequently seen in Polish Jews. It attacks the feet and hands and gradually extends up the limbs. The skin involved in this disease in the most typical cases is bluish-red and the nodules, which tend to become confluent, vary in size from a split pea to a hazelnut. The tumor-nodules are very vascular and on microscopic examination resemble spindle-cell sarcomata. The coloration is due to blood, so that this disease is quite different from melanoma. Kaposi gives excellent colored representations of the diseased parts in his "Handatlas der Hautkrankheiten," Leipzig, 1900, Tafeln 301 und 302.

Chloroma (Green Tumors).—This is an exceedingly rare disease in which sarcoma-like masses form on the bones of the skull and face, especially in the neighborhood of the orbits, and infect other organs secondarily. After death the color of the tumor-like masses is grass-green. The nature of the disease is obscure: some writers regard it as a form of leukemia. It has been carefully studied by Melville Dunlop.

Xanthoma.—Xanthoma with its many synonyms is a curious harmless pigment disease, especially liable to appear in the skin of the eyelids near the inner canthus, hence it is often called xanthelasma palpebrarum. Histologically it consists of a fibrous and fatty tissue containing yellow pigment and connected with the corium. In the eyelids the disease is usually symmetrical and occasionally congenital. These early cases have led some observers to regard the disease as allied to nævi.

Xanthoma may occur on any part of the skin (xanthoma multiplex) and in many instances is associated with jaundice and disturbance of the liver.

The orange-colored pigment is interesting from a physiologic point of view in connection with the oil gland of the rhinoceros hornbill (*Bucorvus abyssinicus*). In this bird the gland secretes an orange-colored greasy matter with which it preens its feathers.

The only normally pigmented tissue found in the human body resembling the yellow and orange of xanthoma patches is the lutein tissue found in the corpus luteum and the walls of lutein cysts arising therefrom.

Pigmentation of the Skin Associated with Tumors of the Adrenals.—Malignant tumors arising in the adrenals of infants (suprarenal capsules) have been described as sarcomata by Greenhow, Hale White, Dalton and others, in infants. The disease may be unilateral or bilateral and is often accompanied by an overgrowth of hair over the surface of the body and a peculiar coloration of the skin. This change in the color is described as a "coppery hue," unlike the bronzing of Addison's disease; and Colcott Fox, in referring to a case observed by Dickinson, writes, in reference to an adrenal sarcoma in a child of three years, that she had an extraordinary development of hair and a "gipsy color" without bronzing.

Sarcomata of the adrenals in childhood are occasionally associated with precocious development of the sexual organs.

Primary cancer of the *pancreas* is accompanied by a peculiar brown coloration of the skin, masking the jaundice. When the gall-bladder is anastomosed with the bowel, the brown pigmentation persists: it is not unlike the brown staining which occurs in the course of pregnancy.

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Neuromata and Neurofibromata.—Surgeons have usually grouped together under the heading *neuromata* all tumors of nerves, but this arrangement has never satisfied pathologists. A large amount of careful investigation has been conducted on the histology of certain lesions of nerves and skin which enables some remarkable and apparently diverse conditions to be covered by the term neuromata. The brain and spinal cord; the roots, trunks, and terminal twigs of nerves; the sympathetic nerve-cords and their ganglia, are all pervaded with connective tissue varying in degree of fineness; for instance, it is coarse in the great sciatic nerve, fine in the brain, where it is termed neuroglia, but of extreme delicacy in the retina.

The common and familiar swelling to which the term neuroma is usually applied is an oval encapsuled tumor composed of tissue indistinguishable from that of the nerve-sheath. These tumors may occur singly or in multiples upon any nerve or nerve-root. Some of them are no bigger than cherry-stones. When one grows on the terminal twig of a cutaneous nerve it gives rise to so much pain, which is often like an electric shock, when touched that it is called in consequence "a painful subcutaneous tumor". (Wood, 1818).

Neuromata form on any nerve, cerebral, spinal, or sympathetic, and on any part of it from the roots to the final terminations. Some nerves are much more liable to be attacked than others, and the tumors vary in size from the head of a pin to the dimensions of a fist. No genus of tumors so thoroughly illustrates the baneful effects of environment as neuromata.

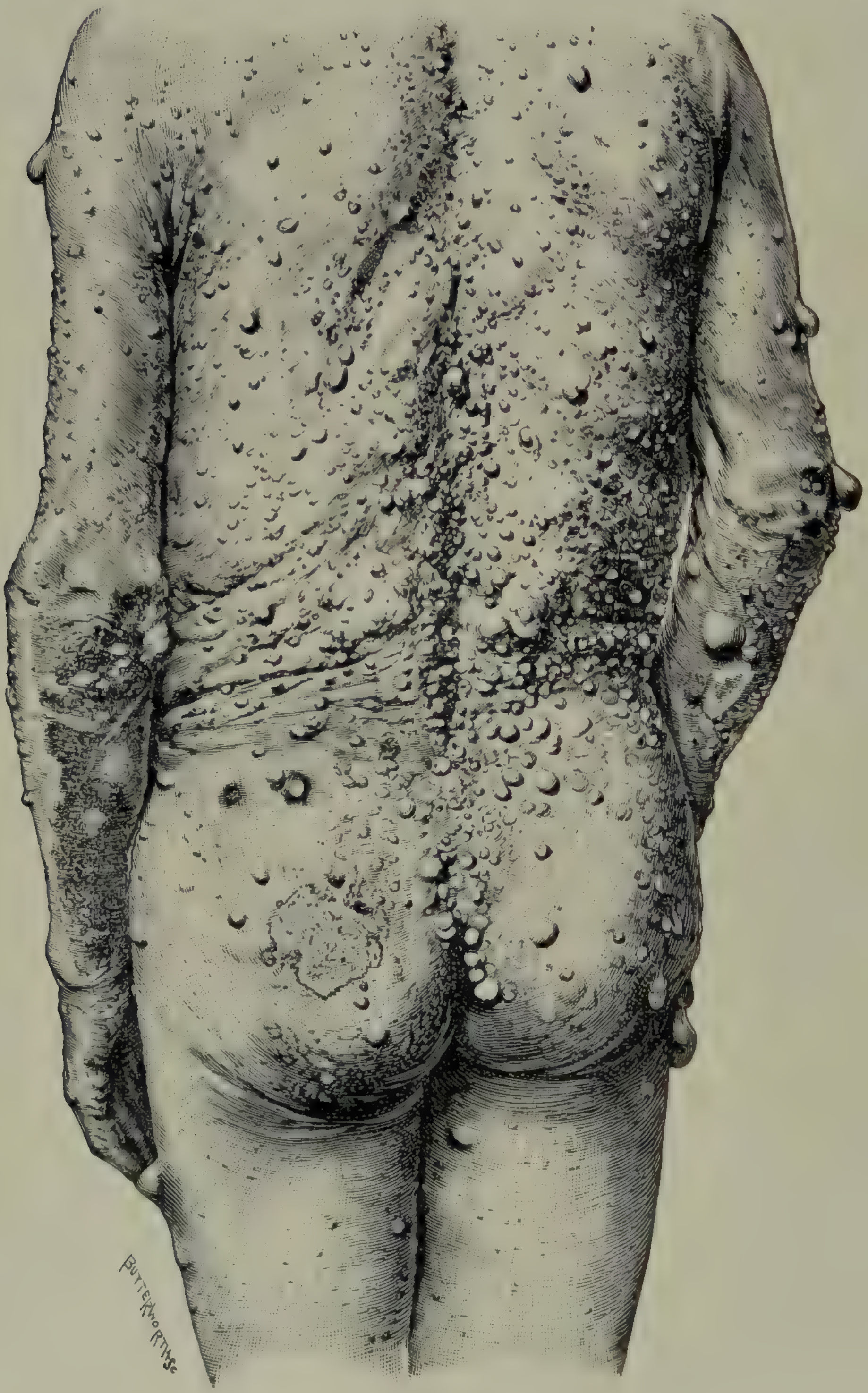

Fig. 197.—Multiple Molluscum Fibrosum (after Payne).

Thus a tumor on the root of a spinal nerve in the cervical region will destroy life before it attains the dimensions of a sparrow's egg, but one the size of a turkey's egg in the great sciatic will cause inconvenience only when the patient sits upon it. A neuroma of the Gasserian ganglion will produce extreme agony (see p. 767) and one on the internal branch of the superior laryngeal nerve will be painless and cause no inconvenience until it interferes with the larynx. The vagus nerve and its branches are liable to be the seats of neuromata. The nerves of the limbs are more prone to neuromata than those of the head and trunk. These tumors are usually encapsuled, and do not, as a rule, mingle with the nerve-bundles.

The common solitary neuroma has received a variety of names depending on its minute structure, such as myxoma, myxofibroma, fibroma and so on, the varieties in texture being due to degenerative changes in the tissue of tumor. It has been definitely proved that multiple tumors sometimes arise in the skin and resemble lipomata, but on careful examination they have been found to contain nerve-elements and particular nerve-cells. These are known as ganglionic neuromata, and it is supposed that they arise on the terminal twigs of the sympathetic nerves distributed to the cutaneous branches of arteries.

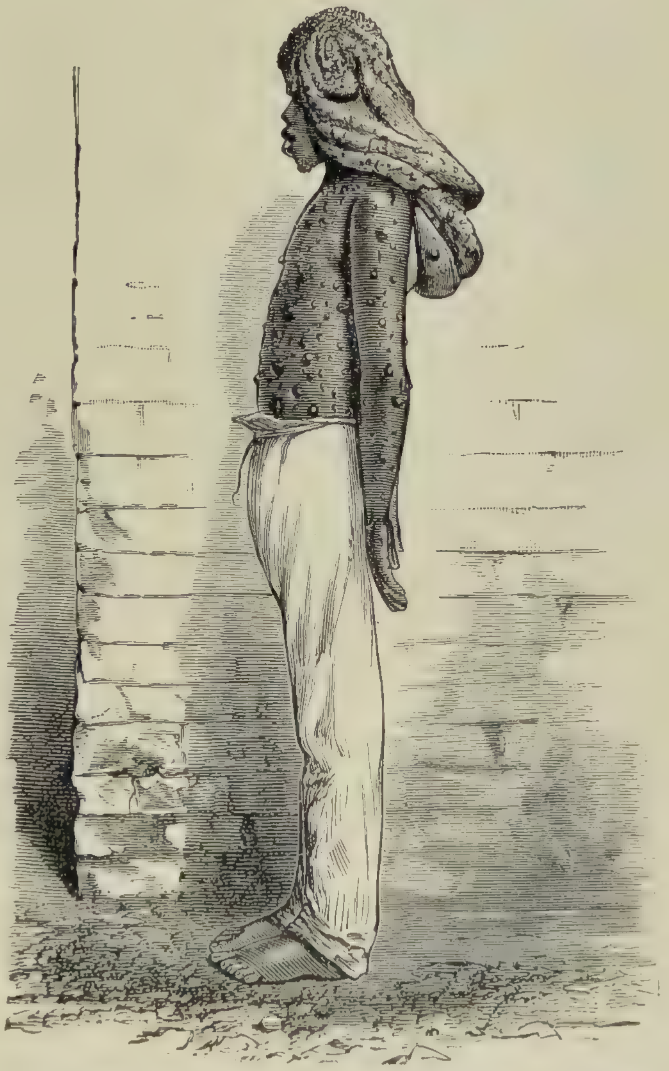

Fig. 198.—A Native of Sierra Leone, Aged Fifty Years, with Molluscum Fibrosum.

The tumors, which were congenital, varied in size from a peppercorn to a billiard-ball (Lamprey).

Men and women occasionally come under observation with tracts excessively developed and forming overlapping folds, either on the trunk and buttocks, the head or limbs. This condition has been described under a variety of names, but that accepted by recent writers is *molluscum fibrosum*. This disease may also manifest itself in the form of a multitude of discrete nodules in the skin varying in size from a mustard-seed to a billiard-ball. Recklinghausen studied the histology of these nodules with very great care and expressed the opinion that they arise from the terminal twigs of cutaneous nerves. Molluscum nodules occasionally occur in persons who have also a multitude of irregular swellings on their nerves, and in one classic case two thousand tumors were observed on the skin and nerve-trunks of one man (Smith).

Though neuromata, molluscum nodules, and molluscum folds occur, as a rule, as separate conditions, nevertheless any two or all three varieties of the disease may coexist.

It is now usual to speak of the generalized form of this disease as neurofibromatosis, and an important feature connected with extreme forms of the disease is the liability of the patient to sarcoma; this may develop primarily, or arise apparently as a malignant change in a molluscum nodule which has existed many years. In some cases of generalized neurofibromatosis the patients die from gradual exhaustion the consequence of ulceration and sepsis in the large pendulous folds of skin.

Glioma of the Brain.—Pathologists have long been familiar with a peculiar overgrowth of the delicate connective tissue of the brain and spinal cord under the name glioma. This appears as a translucent swelling imperfectly demarcated from the surrounding tissue, and, as a rule, this gliomatous tissue has little more consistency than vitreous humor; microscopically it has all the characters of neuroglia. Virchow pointed out that when a glioma is situated near the surface of the brain it appears like a colossal convolution, and when it attacks an optic thalamus this structure will bulge into the ventricles as though overgrown. Occasionally the disease attacks the cerebral crura, particularly in children under twelve years of age, and produces peculiar enlargement of this part of the brain.

Glioma of the Spinal Cord.—This is a rare form of tumor, and judging from the scanty records it would appear that a glioma in the brain is twenty times more common than in the cord. The peculiar relation of gliomatous tissue to the nerve tissue of the cord precludes surgical interference.

Plexiform Neuromata.—It is noteworthy that the connective tissue, more especially the endoneurium of nerves, is liable to a similar gliomatous change; this may be and is usually limited to a particular nerve and its branches, *e. g.*, the anterior crural, the musculospiral, or the great occipital. The effect is very striking, for the nerve becomes thickened, elongated, and tortuous, and when cut across the nerve-sheath is found filled with gelatinous tissue and resembles the section of an umbilical cord. Microscopic examination of the enlarged nerve shows the axis-cylinders embedded in overgrown endoneurium. To this condition the name plexiform neuroma is applied. This disease is congenital, and the skin overlying the affected nerves is often brown and even hairy, and resembles the condition known as a hairy and pigmented mole.

The plexiform neuroma is not only allied to gliomata by the peculiar changes in the endoneurium, but its pathologic relationship to molluscum fibrosum and localized neuromata is sometimes demonstrated by the occurrence of a plexiform neuroma beneath a molluscum fold; and a large oval neuroma may be found on the trunk of a nerve the sheath of which is irregularly thickened throughout.

There are good reasons for including retinal gliomata in this group, for the optic nerve and retina are primarily a process of the brain, and the parallel exhibited in the age distribution of gliomatous enlargement of the pons and crura cerebri and limitation of glioma of the retina to children under twelve years of age are significant facts. The malignancy of retinal glioma has its parallel in the occasional occurrence of sarcoma in a molluscum nodule.

Tumors of the Optic Nerve.—These are very rare, but they are described under a variety of titles, such as glioma, myxoma, myxosarcoma, fibroma, and sarcoma. Such tumors are unilateral and the greater proportion occur before the twentieth year of life. The optic nerve is a complex structure and in the embryo is preceded by an outgrowth from the brain known as the optic stalk; this stalk is ultimately replaced by a fibrous nerve, the nerve-elements of which are in part derived from the retina and part perhaps from the brain. Thus the early tissue of the optic stalk is identical in structure and continuous with the sustentacular tissue of the embryonic retina.

These facts are of importance because in some cases, especially in adults, sarcomata arise from the sheath of the nerve, and do not primarily involve the nerve fibers. Pockley has excised a tumor from the optic nerve, and saved the nerve and the globe. The patient was a boy of nineteen years. The tumor is described as an encapsuled round-celled sarcoma. Some recently recorded cases which have been very carefully investigated point to the conclusion that many of the tumors arising within the sheath of the nerve, especially in children, are particularly connected with the pial sheath, and in construction are closely allied to, if not identical with, the retinal (glioma) sarcoma of infancy. The malignancy of optic nerve sarcomata, though pronounced, is not excessive.

Tumors of the optic nerve are usually ovoid in shape, with their long axes coincident with that of the nerve. Their surfaces are usually smooth, and in size they vary greatly, but rarely exceed a pigeon's egg. They do not tend to invade the globe, but they are apt to creep through the optic foramen and involve the intracranial portion of the nerve. As the fibers of the nerve are early implicated, vision is soon interfered with; there is proptosis, but the movements of the eye are free, and there is no pain, even on manipulation.

Much of the confusion relating to the nomenclature and structure of tumors of the optic nerve is due to their rarity.

Glioma of the Retina.—In structure these tumors mimic the granular layer of the retina, and Treacher Collins has drawn attention to the great similarity which exists between the cells composing the retina of the fetus at the third month, when its layers are undifferentiated, and the tissue of a retinal glioma.

This tumor occurs exclusively in children; exceptionally it has been detected at birth, more commonly it makes its appearance during the first four years of life; it is very rare after the seventh year, and is almost unknown after the age of twelve. In a certain proportion of cases (20 per cent.) both retinæ are affected, either simultaneously or after a brief interval. This is always an indication that the tumor is highly malignant. In the early stages there is, as a rule, no pain or symptom denoting the presence of a tumor; gradually the pupil dilates, and a peculiar reflex is noticed at the fundus (this is often termed cat's-eye), and, on testing, the eye will be found quite blind. As soon as the existence of a glioma is discovered by the surgeon, the eye is, as a rule, promptly excised. In cases where treatment of this kind is refused or deferred, the following changes occur. The tumor, continuing to increase, pushes forward the intra-ocular structures and induces great pain as the result of the increased intra-ocular pressure it produces, until the cornea yields and the tumor bursts forth, and, growing very rapidly, soon makes its way between the eyelids, which become swollen and everted, and then, in consequence of exposure, assumes a dusky red fleshy appearance, while from its surface a sanious fluid exudes which may form crusts on the surface of the tumor. Should the parts become excoriated or be handled, they bleed freely. A fungating tumor of this kind will sometimes attain a very large size before it destroys the child's life.

After excision of an eye for retinal sarcoma the disease is very prone to recur, and the recurrent tumor may attain very large proportions before it destroys life. When the operation has been long delayed, the growth may have burst through the sclerotic and invaded the orbital tissues; in a larger proportion of cases it has infiltrated the optic nerve, and it is in this structure that the disease reappears. The frequency with which sarcoma returns in the stump of the optic nerve is, in all probability, due to the intimate lymphatic relations of this nerve with the intra-ocular lymph spaces.

In regard to the question whether "glioma" may "run" in a family, there is little evidence to guide us. Fuchs has recorded a case where two children were affected in one family, and two very extraordinary reports have recently come from Australia. Earle Newton states that in a family of sixteen children ten died from retinal glioma; three of the cases were unilateral and seven bilateral. All the affected children, with one exception, died about the third year. Maher tells of a family of four children of whom three died of glioma, and in two it was bilateral.

Dissemination of retinal sarcomata is exceptional. The common situations for secondary deposits are the brain, the lymph glands about the jaws, and the periosteum of the bones of the skull.

The *treatment* for retinal sarcoma is removal of the eye, and the importance of promptness in this matter is indicated in the careful inquiry conducted by Lawford and Collins. They prove very clearly the following points:

The quicker an eye is removed after the discovery of the disease, the better the prospect of cure. In the majority of cases the disease returns in the orbit, and in a very small proportion of cases secondary deposits occur in other parts. When recurrence takes place it is rarely delayed beyond nine months; but one undoubted case has been reported in which the disease returned three years after the primary operation. If three years elapse and there is no recurrence, the recovery may be regarded as permanent. Out of fifty-four cases in Lawford and Collins's list, eight patients were alive and free from recurrence three years after the removal of the eye for retinal glioma: this, in comparison with the inquiries of others, would seem to indicate the proportion of successes. It is significant to note that in seven of these cases the disease affected one eye only. This shows the almost hopeless condition of the patient when both eyes are affected.

Other statistical inquiries have been conducted with the view of obtaining the percentage of cures in this disease, and they work out at about the same proportion as in the paper mentioned above.

Clinical Features of Neuromata.—Neuromata are, in the majority of cases, innocent tumors; they very rarely recur or become disseminated; nevertheless they are in exceptional cases the cause of death. A large intracranial neuroma will produce fatal pressure on the brain, and several cases are recorded in which small neuromata of the spinal nerve roots have caused paraplegia and death. Smith refers to a case in which a woman complained of severe pain in the course of the right trigeminal nerve; this pain was so much increased by mastication that she ate but little, and speaking aggravated it to such a degree that she always remained silent unless interrogated, and even on these occasions she frequently replied by signs. She died after enduring severe and uninterrupted pain during four and a half months. At the autopsy a neuroma as large as a walnut occupied the situation of the right Gasserian ganglion. With modern methods of surgery no person will be allowed to suffer in this awful manner. The difficulty of treating such cases is shown in a specimen figured by Lexer. A woman aged seventy-three died after resection of the Gasserian ganglion for severe trigeminal neuralgia. At the examination after death a tumor the size of a walnut was found surrounding the trigeminal nerve before it entered Meckel's cave.

The pain produced by pressing a painful subcutaneous tubercle has already been considered. When the roots of the spinal nerves are involved in a neuroma, pain is a prominent symptom, until the tumor is large enough to compress the cord and produce paralysis: these signs, however, are not peculiar to neuromata of the spinal nerve roots.

Neuromata of the nerves of the limbs are usually solitary, ovoid, the long axis of the tumor coinciding with that of the limb, and always painful when pressed, the pain radiating throughout the distribution of the nerve below the point of attachment of the neuroma.

Treatment of Neuromata.—A solitary neuroma in an accessible position is easily removed. When seated upon a large nerve-trunk, especially if it contain motor fibers, care must be exercised to avoid damage to the nerve. In many cases the tumor can be separated without injury to the nerve. Keen succeeded in enucleating three neuromata from the ulnar nerve in the palm. It occasionally happens that the neuromatous nature of the tumor is not recognized until after its removal with a portion of the nerve. In the limbs such breaches in the continuity of nerves have been repaired by grafting fragments of nerves from amputated limbs or from rabbits; it is, however, always better to avoid the accident by careful surgery than to remedy it by secondary measures, however brilliant. Persistent facial palsy has followed removal of a neuroma lodged in the parotid gland. Neuromata within the spinal canal have been successfully removed. A neuroma of the optic nerve usually necessitates excision of the eyeball. Chavasse removed a large neuroma from a cervical nerve; septic spinal meningitis followed, ending in death.

Multiple neuromata, and especially those associated with molluscum fibrosum, are beyond the reach of surgical art.

Plexiform neuromata have been several times successfully removed; exceptionally, when affecting the nerves of a limb, amputation has been necessary. This form of neuroma on the lingual nerve has caused enlargement of the tongue simulating macroglossia, for which excision of the tongue was performed (Abbott and Shattock).

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Angeiomata and Tumor-diseases of Blood and Lymphatics.— These are tumors composed of an abnormal formation of blood-vessels. This genus contains three species. (1) Simple nævus; (2) cavernous nævus; (3) plexiform angeioma.

The simple nævus is very common and appears on the skin and occasionally in mucous membrane as a patch of discoloration which may be pink or deep blue. When the abnormal vessels in a nævus are mainly venules it will be blue, but when arterioles preponderate it will be pink. The vessels of a nævus are embedded in fat and a few lymphatics are present; when the lymphatics are more numerous than the venules and arterioles the patch is called a lymphatic nævus, or lymphangeioma.

Nævi vary in size: some are scarcely perceptible, while others involve the skin of half the face, trunk, or the greater part of a limb. They are often multiple and occur in any part of the skin, lips, labia, conjunctiva, or tongue. Small nævi tend to disappear; some remain stationary and a few become converted into cavernous nævi. These are sometimes called erectile tumors because they structurally resemble the cavernous or erectile tissue of the penis.

Cavernous nævi are common on the skin, and they have been observed in the rectum, subperitoneal tissue, liver, larynx, bladder, the wall of the right auricle of the heart, and in voluntary muscles, such as the deltoid, gracilis, and the semi-membranosus.

The plexiform angeioma or "aneurism by anastomosis" of older writers consists of a number of abnormal blood-vessels of moderate size arranged more or less parallel to each other, as in the *retia mirabilia* in the fore-limbs of sloths, or the tail of the great anteater, etc. Some plexiform angeiomata are made up of arteries only, others of veins and arteries. The component vessels are often tortuous. Fortunately this species of angeioma is very rare; it has been observed on the scalp, in the orbit, on the forearm, and in the perineum surrounding the urethra.

All angeiomata are congenital or arise in the first few weeks after birth: it is instructive to watch a small red fleck, at first no larger than a split pea, slowly spread and then begin to stand above the level of the skin; a few months later it may form a raised pulsating lump which may be red or blue according to its primary connection with arterial or venous vessels, and at last requiring some courage as well as skill on the part of the surgeon who attempts to operate upon it.

Occasionally a simple nævus will become converted into a cavernous nævus and the central parts of the latter fuse and form a central space so that the tumor resembles a cyst with very vascular walls. Such are sometimes called nævoid cysts.

(The treatment of nævi is considered in detail in Vol. II.)

Lymphangeiomata.—The tumors are due to abnormal formation of lymphatics and bear the same relation to lymph vessels that angeiomata bear to the hæmic capillaries. There are three species: (1) Lymphatic nævus; (2) cavernous lymphangeiomata; (3) lymphatic cyst.

The lymphatic nævus is almost colorless, but as it contains hemic capillaries it may be a pale pink: in the mucous membrane of the tongue it is sometimes of a faint yellow or of the color of serum. When a lymphatic nævus affects the lingual mucous membrane and becomes cavernous it produces great enlargement of the tongue—*macroglossia*—and causes it to protrude from the mouth, which is no longer capable of containing it. When the mucous membrane of the lip contains a lymphangeioma it enlarges and causes the deformity known as *macrocheilia*.

As in the case of angeiomata, a cavernous lymphangeioma may become cystic in the center and form a cyst, but the most typical lymphatic cysts occur in the neck as congenital swellings commonly known as "hydroceles of the neck." They appear as translucent swellings, and though most frequent in the neck are also found in the axilla and on the anterior and posterior walls of the thorax. These cysts are filled with lymph and the walls contain nævoid material. The most remarkable fact in connection with them is their great tendency to disappear: they are excessively prone to inflame, and this event usually precedes their disappearance. In some of the recorded cases it is stated "that the cyst was burst by the child falling upon it," and the accident induced its cure. The proneness of lymphatic cysts to undergo spontaneous cure during childhood explains their rarity after puberty: this is fortunate, for their treatment by surgical means is uncertain and often dangerous.

Endothelioma.—Tumors to which this name is applied are supposed to arise from the inner walls of blood and lymph vessels, and from the surface of serous membranes, such as the peritoneum, pleura, and dura mater.

Endotheliomata do not, as a rule, attain a large size, but are prone to degenerate: they are malignant, but display this evil propensity more especially in the form of local recurrence. These tumors occur particularly in the muco-periosteum of the jaws (gums), palate, and the skin in connection with moles and warts. It is probable that many tumors described as squamous celled cancer (epithelioma) of the gums and palate, and the remarkable tumors described as cystic disease of the jaws, and some malignant tumors of the lining membrane of the antrum and of the mucous membrane of the nasal septum are endotheliomata.

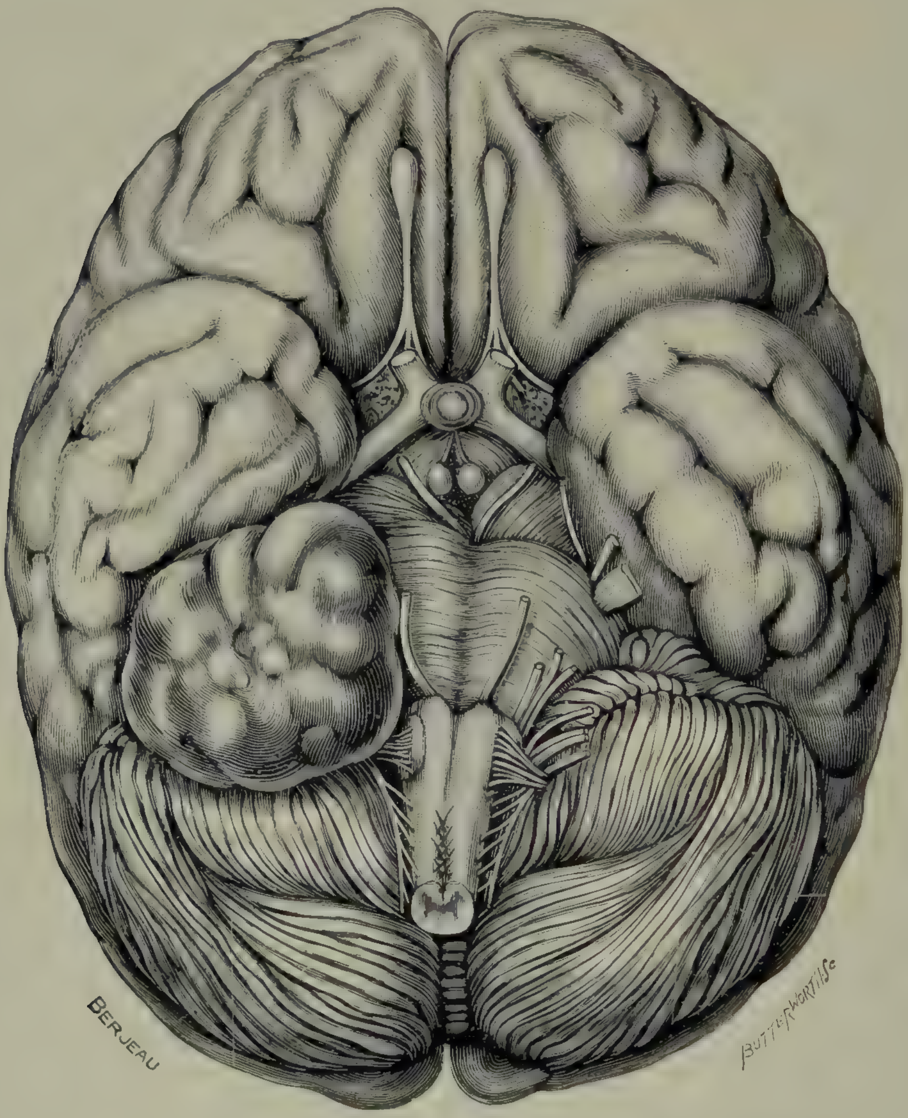

Fig. 199.—A Psammoma (Endothelioma) in Relation with the Flocculus.
From a man thirty-six years of age who died after an attempt to remove the tumor. Its chief symptoms were pain, headache, vomiting, giddiness, deafness, and nystagmus.

Some of the curious tumors of the parotid and submaxillary salivary glands usually described as sarcomata, but puzzling on account of the variety of the component tissues, belong to this genus. The clinical course of these tumors displays as much vagary as their structure.

Endotheliomata are divided into species according to their origin; hæmendotheliomata arise in blood-vessels, whilst lymphendotheliomata grow from lymphatics. The peritheliomata, a remarkable variety detected by Ziegler and named by him angeio-sarcomata, when examined under a low power of the microscope recall superficially the lobulated structure of the liver. On closer examination it will be seen that this peculiar structure depends upon cellular overgrowth of the perivascular sheaths of the small vessels. The abnormal tissue forms a cell-mantle, so to speak, around the vessel, much in the same way that the axis-cylinders of nerves are swathed in myxomatous tissue in the condition known as plexiform neuroma:

A fourth variety, the *dura-endotheliomata,* includes the remarkable tumors which grow from the membranes of the brain and spinal cord; they are commonly known as *psammomata* (sand tumors) which grow in connection with the choroid plexuses of the cerebral ventricles and especially in the neighborhood of the flocculus at the point where the choroid plexus of the fourth ventricle emerges from the cornucopiæ.

Fibroids of the Uterus.—The tumors of the uterus known as fibroids, myomata, and fibromyomata are extremely common, and on account of the difficulties and dangers which arise from them directly and indirectly they have been carefully studied. They arise in any part of the uterus, but are more frequent in the body of the organ than its neck. A uterus may contain one fibroid; more often they are multiple; one hundred and forty is the greatest number I have counted in one uterus. In their early stages they look, on section, like knots in a piece of wood, and are always encapsuled. When projecting on the peritoneal surface of the uterus they are said to be subserous; when completely embedded in the uterine wall, fibroids are said to be intramural, and when projecting into the cavity of the uterus, submucous. If they hang from the endometrium by a narrow portion like a stalk, they are often called polypi.

The fibroids which grow in the neck of the uterus and attain a diameter of 10 cm. assume a characteristic ovoid form.

Uterine fibroids differ much in texture: some are as hard as cartilage, and a few, when calcified, resemble porous stone; others are as soft and succulent as a ripe orange, and occasionally some are equal in consistence to jelly. Between these extremes every degree of hardness or softness occurs, but they all agree in one particular—namely, in the possession of a well-developed capsule, a structure of vital importance to a fibroid, as its life depends upon it. Hard fibroids are yellowish-white on section, softer specimens resemble the normal color of the uterus and often present on the cut surface a whorled appearance. Soft tumors, as a rule, grow quickly, and are very vascular, but the hardest and the gelatinous fibroids are poorly supplied with blood.

Attention has already been drawn to the fact that the only structural feature fibroids have in common is a well-marked capsule, of fibrous tissue, which completely isolates the tumor proper from the uterine tissue. Even in completely calcified fibroids a thin capsule can be demonstrated, and occasionally the only solid representative of the fibroid is the capsule, the originally solid parts of the tumor having slowly liquefied. Fibroids changed in this way are often referred to as "fibrocystic" tumors.

The most typical variety of "fibroid" not only resembles the wall of the normal uterus in toughness, but is similar to it in microscopic structure, and consists of unstriped muscle tissue, which has a remarkable tendency to be arranged in whorls.

The very dense fibroids are composed of tissue which microscopically resembles dense fibrous tissue, with here and there strands of cells resembling unstriped muscle cells. This variety is often called *fibromyomata*, and its members display the whorled arrangement in a very striking manner. The fibromyomata are very liable to calcify.

The soft, jelly-like fibroids are, in the majority of cases, due to secondary (myxomatous) changes in tumors which were originally hard. This is proved by the fact that patches of softening are found in hard tumors, and occasionally fibroids come to hand in which the very hard, calcified, gelatinous, and diffluent tissues coexist. However, it is important to remember that these changes do not always depend on the age of the tumor, for a very large proportion of uterine fibroids which occur before the thirtieth year are myxomatous, and, what is more important, these soft (almost liquid) fibroids are locally malignant—that is, they recur if enucleated, and this sometimes happens very quickly.

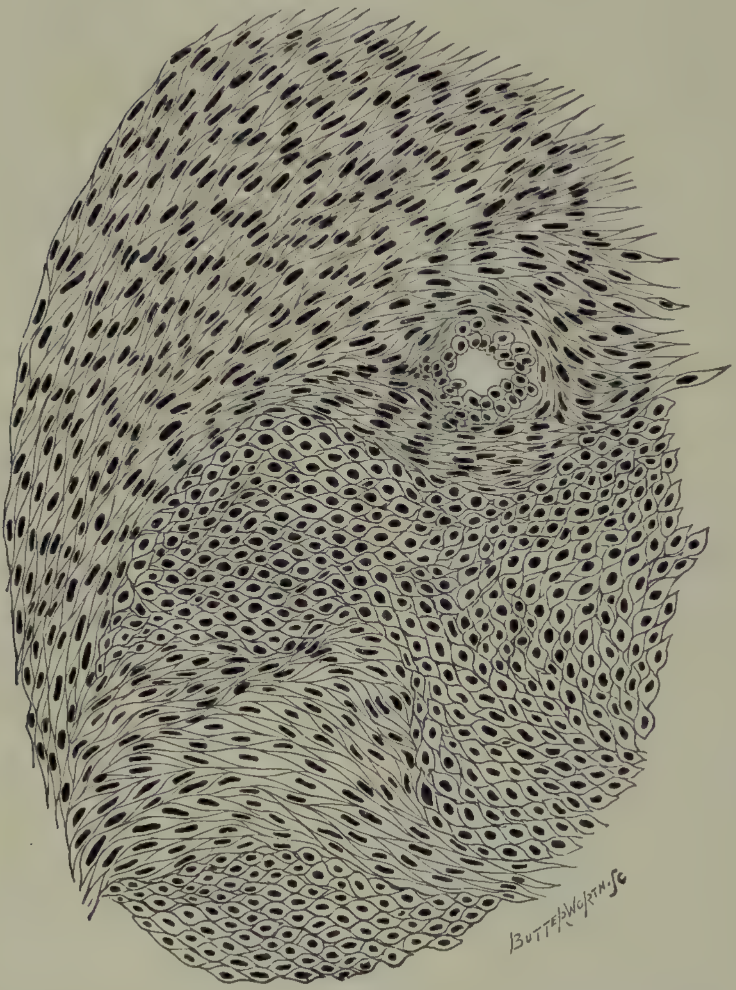

FIG. 200.—THE MINUTE STRUCTURE OF A YOUNG UTERINE FIBROID.

The circular cells are spindle cells cut at right angles. This figure represents a complete section through the equator of a seedling fibroid the size of a mustard-seed. ("British Medical Journal," 1901, i, 814.)

A woman may have many hard fibroids in her uterus and not feel any inconvenience, but when the tumor is of soft jelly-like consistence her health undergoes marked deterioration quite apart from the menorrhagia caused by the tumor.

Malignant Changes in Fibroids.—It is believed by many that a sarcomatous change may arise in uterine fibroids. The matter has been carefully considered by competent men, and a critical examination of the evidence makes it clear that in a very large proportion of the cases described as "sarcomatous degeneration of a fibroid" the changes were due to septic infection. In all future records published as evidence in this direction there must be a careful account of the minute structure of the tumor by a competent pathologist. The great defect in nearly all the recorded cases in which the malignant change has been suspected is the absence of any description of the mode of death where the patient survived the operation. Sarcomata are so prone to disseminate that any patient who has died in consequence of malignant degeneration of a fibroid would be expected to have secondary nodules in the lungs at least.

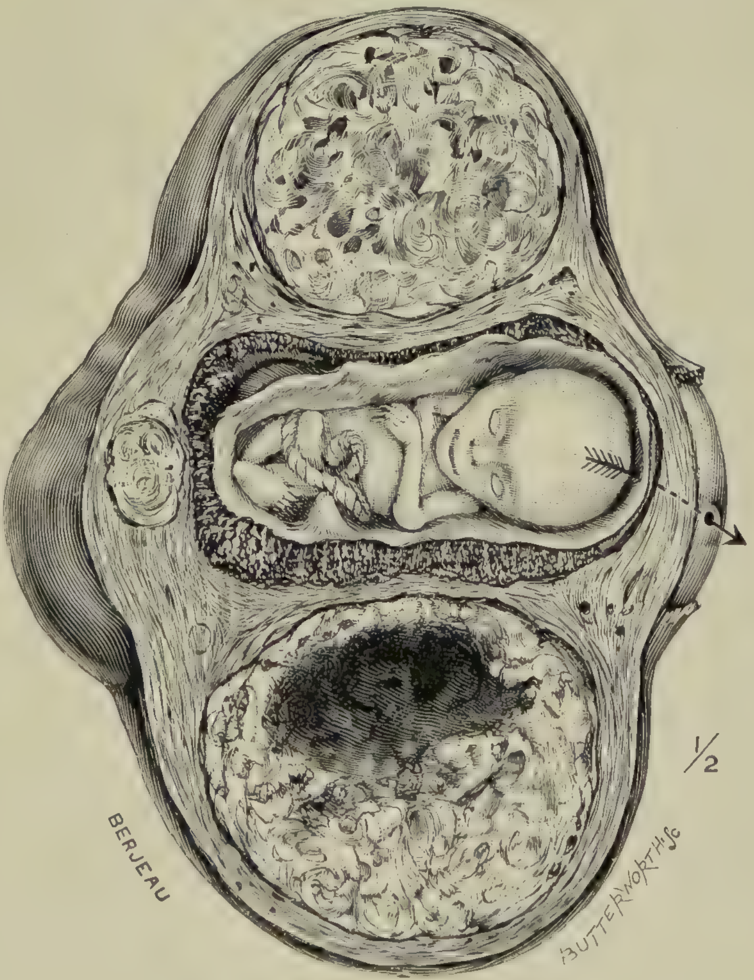

Fig. 201.—A Gravid Uterus in Section.
The fibroids have undergone softening and red degeneration.

Pregnancy is very inimical to fibroids and produces some curious changes in them, such as edema from interference with the circulation in the fibroids, softening, and often liquefaction of the tissue. In addition to these alterations the tumor often undergoes a marked change of color.

The usual color of a uterine fibroid is pale yellow; in many degenerating and necrotic fibroids this color deepens. In the course of pregnancy a fibroid, especially one of the interstitial kind, assumes a deep red or mahogany tint. In the early stages the tumor exhibits the color in streaks, but as the pregnancy advances it permeates the whole tumor. Occasionally, even in the mid-period of pregnancy, this necrotic change may be so extreme that the central part of the tumor is reduced to a red pulp.

In 1903 Fairbairn wrote an excellent paper on this necrotic change in fibroids, and it is now becoming familiar as the "red degeneration." Until Fairbairn began to accumulate the material for this paper I held the opinion that this change was only seen in association with pregnancy, but he soon convinced me that it occurred in spinsters, and I have myself seen since well-marked examples in women who have never been pregnant. At the same time it must be stated that the largest numbers, the best marked, so far as color goes, and the most extreme examples of this red degeneration occur in association with pregnancy.

In the early cases which came under my notice the redness of the cut surface of these tumors so strikingly resembled beef-steak that it suggested to me, and appears to have done so to other observers, that the change in color might be due to an increase in the muscle fibers in consequence of the physiologic enlargement of the uterus. The microscope, however, dispelled this illusion, showing the coloring material to be blood pigment diffused through the necrotic tissue of the tumor.

It is too true that fibroids are the commonest of all the species of tumors to which women, whether married, single, fruitful or barren, are liable. It is also a fact that the uterus may contain one fibroid or many and cause neither inconvenience nor suffering—indeed, the individual owning them may be ignorant of the existence of a tumor in her womb; but it is equally true that they are often the source of much suffering, and occasionally cause death in insidious ways, some of which will be considered.

Hemorrhage is the commonest of all the inconveniences which fibroids cause, but it is confined to those which implicate the endometrium. The bleeding occurs under two conditions; most commonly it takes the form of excessive loss at the normal menstrual periods (menorrhagia). The most serious hemorrhages are associated with septic changes in the tumor. It is a fact of some importance that a small submucous fibroid will induce such profuse bleedings at the menstrual period as to place life in imminent peril, while a large interstitial tumor, even though it project into the uterine cavity, scarcely influences the loss.

When a woman with a fibroid bleeds excessively between as well as at the normal menstrual periods, it often indicates that the tumor has become septic.

It is important to realize that oft-repeated losses of blood continued over a long period not only lead to profound anemia, but also to grave changes in the heart muscle, which frequently end in sudden death, as well as greatly adding to the operative risks when such individuals submit to surgical procedures.

Septic infection is the most serious complication of uterine fibroids, and even when it does not cause death is always attended with the most dangerous consequences.

Fibroids are liable to become impacted in the pelvis and give rise to troublesome pressure on the rectum, bladder, and ureters, leading to dilatation of the pelves of the kidneys. The most insidious forms of pressure are associated with large fibroids of the cervix. It is one of the most striking features of the cervical fibroids that they rarely cause bleeding except when they extrude from the mouth of the uterus and become infected, and cause inconvenience only when they interfere with the bladder. Herein lies the danger, as grave injury is often wrought on the pelvis of one or both kidneys before the existence of the tumor is even so much as suspected. It is an important fact to remember that *when a woman between thirty-five and forty-five seeks relief because she suffers from retention of urine for a few days preceding each menstrual period, it is almost certain that she has a fibroid in her uterus.*

A uterus occupied by fibroids is sometimes passively rotated as the tumors grow, but pedunculated fibroids sometimes undergo acute axial rotation like ovarian tumors and twist their pedicles.

Intestinal obstruction occasionally arises from the pressure of a fibroid impacted in the pelvis, and the stalk of a pedunculated fibroid may entangle a coil of small intestine: neither accident is common.

Some of the most baleful effects of fibroids are produced when they coexist with pregnancy. Certainly they are unfavorable to conception, they predispose to miscarriage, often hinder or altogether obstruct delivery, and in patients where all these difficulties have been surmounted the tumor is a source of danger during puerpery.

Fibroids and the Menopause.—It was formerly taught and believed that uterine fibroids cease to be troublesome with the cessation of menstruation. It is quite certain that this opinion requires reconsideration. Uterine fibroids stand alone among tumors in the peculiarity of their age distribution, for, as has already been mentioned, they only arise during menstrual life (fifteen to forty-five), but they stand absolutely alone among tumors in possessing another remarkable character: as a rule, they cease to grow after the menopause, and in some instances they undergo a marked diminution in size. Some writers are of opinion that they may disappear. This must be a very exceptional phenomenon, hard to prove and very difficult to believe.

Though fibroids, as a rule, cease to grow after the menopause, it must not be forgotten that they *sometimes take on unusually rapid growth at this period;* and, apart from this, they are often sources of great peril to life by coexisting with other serious diseases of the uterus, tubes, and ovaries, while the very fact that they are apt to diminish in size is occasionally a source of danger. Apart, however, from these considerations, the fibroids are themselves sources of trouble on account of the degenerate and septic changes to which they are liable. It is also very essential to bear in mind that the existence of a fibroid in the uterus has in a very large proportion of cases a malicious influence in delaying the menopause. The uterus has often been removed from patients between the fiftieth and sixtieth years in whom monthly fluxes of blood were as regular but much more profuse than in women of twenty years. On the other hand, occasionally a woman may have her menopause at the forty-second or forty-fifth year, though a large fibroid is connected with the uterus.

The fact that a fibroid may shrink after the menopause is in itself frequently a source of danger, especially when pedunculated, for the tumor may be so big that its size prevents it from tumbling into the pelvis, but after the shrinking consequent on the menopause, such a fibroid may fall into the true pelvis and become impacted. It is a rare complication, but it happens.

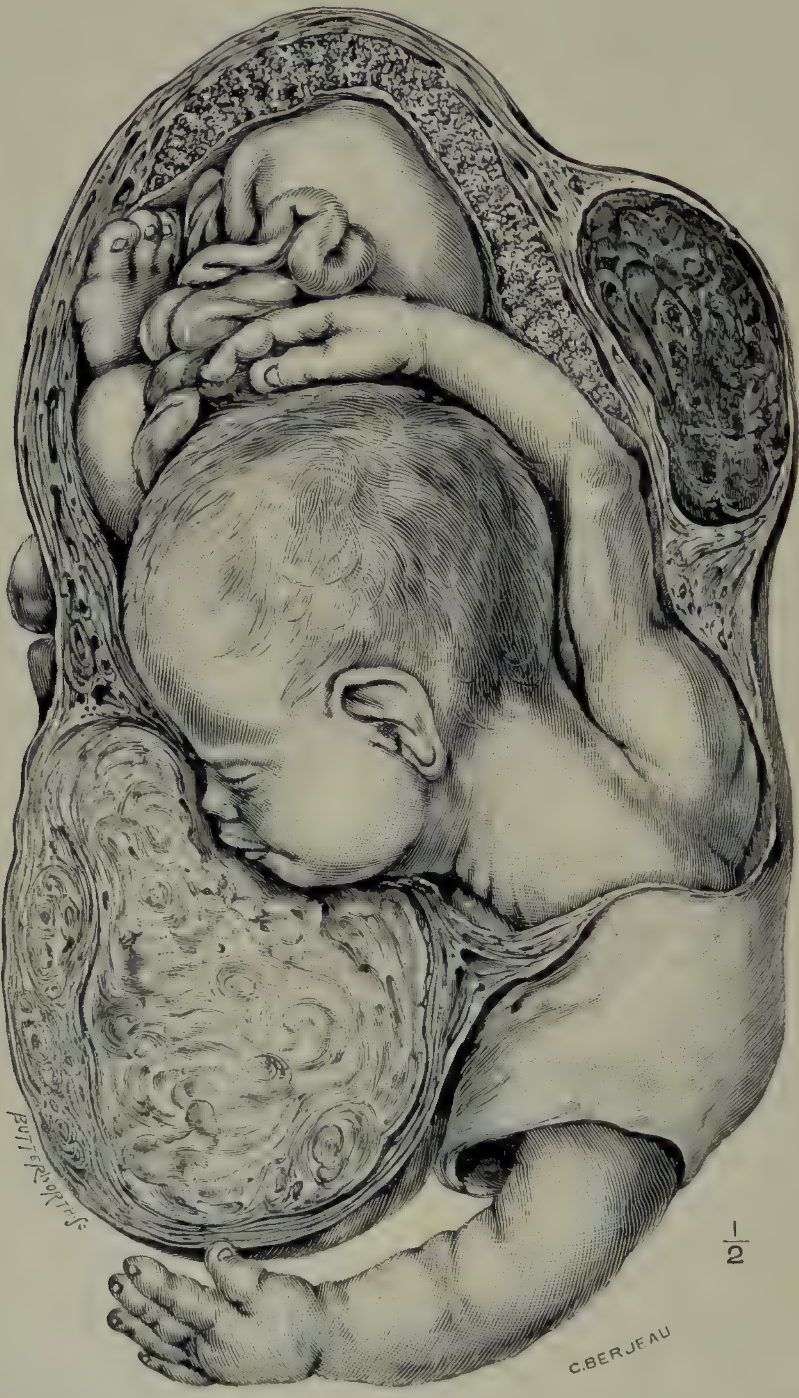

Fig. 202.—A Fibroid of the Neck of the Uterus Obstructing Delivery. Total hysterectomy was performed during labor: the patient recovered.

The most frequent and dangerous alterations in fibroids after the menopause are necrotic and septic changes. During menstrual life fibroids generally enjoy an abundant blood-supply, and in some instances they are almost as vascular as nævi. On the occurrence of the menopause, the cessation of the menstruation is accompanied by a remarkable abatement in the blood-supply, and the tumor not only ceases to grow, or even shrinks, but the very fact that its nutritive irrigation, so to speak, is arrested, leads to degenerative changes, and the fibroid becomes in many instances a dead, sequestered body, and so long as septic organisms are denied access it will remain inert. When from various causes putrefactive organisms gain access to these essentially dead tumors, the results are often dire in the extreme.

It is far easier to prove that putrefactive organisms obtain access to dead or dying fibroids than to tell how they get to them. There is, however, one mode of access which is undeniable. The fibroids which give rise to most trouble after the menopause are those of the submucous variety, and there seems a strong tendency, when the uterus passes into its resting stage and the fibroid is shrinking and dying, for the organ to attempt the extrusion of the tumor. A careful study of the cases which have come under my observation teaches me that a fair proportion of troublesome post-menopause fibroids have undergone partial extrusion, or the mouth of the womb is widely dilated and facilitates the ingress of germs.

It has already been pointed out that one of the greatest perils which can happen to a woman with a fibroid in her uterus is to become pregnant, but after the forty-fifth year she is beset with a complication of quite another kind—namely, cancer of the corporeal endometrium.

Clinical Characters.—Uterine fibroids, though exceedingly common, are unknown before puberty, and rarely attract attention before the twentieth year: they are most common between the thirtieth and fiftieth years. In a large proportion of patients the earliest indication of the presence of a fibroid in the uterus is excessive menstruation (menorrhagia); this is often the only symptom which leads the patient to seek advice, and on examination a large pelvic tumor may be detected. In many cases there is no obvious enlargement of the uterus; the fibroid, though big enough to cause severe bleeding, is not large enough to be detected until the cavity of the uterus is explored through a dilated cervical canal. In many instances when the patient seeks advice the tumor is actually presenting at the mouth of the womb.

Fibroids large enough to rise out of the pelvis usually occupy the hypogastrium, but when stalked they may lie laterally and simulate ovarian tumors. On palpation fibroids may be smooth, but when their surfaces are tuberous it is a valuable sign. Auscultation sometimes furnishes useful evidence, for soft, rapidly growing fibroids often yield a loud hum synchronous with the pulse, like the murmur heard during pregnancy; this venous hum is most frequently detected shortly before the onset of a menstrual period.

On vaginal examination the tumor will be found closely associated, and often incorporated, with the uterus. When the tumor occupies the cervix, the whole organ feels like a globular body and the mouth of the womb is indicated by a mere dimple. The diagnosis of a fibroid in the uterus is often rendered difficult by complications, such as pregnancy—uterine, tubal, or even cornual; the coexistence of ovarian cysts and solid tumors; tubal conditions, such as hydrosalpinx and pyosalpinx and primary cancer of the Fallopian tube; and tumors of the pelvic bones and connective tissue.

Treatment.—All attempts to cure fibroids by drugs or by means of electricity have been conspicuous failures, so that patients whose lives and usefulness are threatened by these tumors are obliged to seek the aid of surgery.

It is true that fibroids often occupy the uterus for years and cause no trouble, but many give rise to severe bleeding and place life in great jeopardy. Recurrent bleeding is the most common condition which leads women with fibroids to seek medical advice. Pelvic pain due to pressure of the tumor on the urethra, bladder, or bowel is common, and inimical to health. Inflammation (infection) and gangrene are dangerous conditions. Fibroids complicated with tubal and ovarian disease demand careful attention. The chief indications for surgical interference may be summarized thus:

1. A stalked tumor protruding at the mouth of the womb is readily detached by seizing it with a volsella and twisting the stalk; or the pedicle may be divided by scissors.

2. The presence of a submucous fibroid is often conjectural; then the cervical canal is dilated and the interior of the uterus explored with the finger. Small fibroids thus discovered are easily removed. Larger tumors require enucleation.

3. Submucous fibroids with a diameter exceding 5 to 6 cm. usually require removal of the uterus (hysterectomy). There is a consensus of opinion among surgeons and gynecologists that hysterectomy for fibroids may be recommended in the following circumstances: (1) When the fibroids cause profuse and long-continuing menorrhagia. (2) When the fibroid is septic and gangrenous. (3) Impacted and irreducible fibroids causing pain and retention of urine. (4) Fibroids which are growing rapidly and those which are degenerate and softened (cystic). (5) Cervical fibroids too large to admit of removal by the vagina. (6) Fibroids complicating pregnancy, delivery and puerpery, in certain circumstances.

It is admitted by most writers that the ideal method of dealing with fibroids requiring removal by celiotomy is to remove them either by ligation or by enucleation, and in certain circumstances by actually opening the uterine cavity, extracting the tumor, and then suturing the incision as after a Cesarean section, an operation to which I applied the term *hysterotomy*. In actual practice this ideal operation of removing the tumors and leaving the uterus and ovaries intact can only be carried out in a small proportion of cases, probably in less than 10 per cent., and it is fair to state that enucleation and hysterotomy are often more troublesome and serious operations than hysterectomy, also the preservation of the uterus is not always an advantage to the patient.

When a woman is submitted to hysterectomy for fibroids we can assure her that the tumors will not recur, but after a myomectomy or enucleation in a woman in the reproductive period of life we cannot give her this assurance, for she may have in her uterus many "seedlings," or what I prefer to call "latent fibroids," and one or several of these may grow into formidable tumors.

In the case of a young woman contemplating matrimony or a married woman anxious for offspring myomectomy is a justifiable operation. Experience, however, teaches this stern lesson: *After the enucleation of a fibroid in the procreative period of life a woman is twenty times more likely to grow more fibroids in her womb than to conceive successfully.*

Another legitimate class of cases in which myomectomy is a very safe undertaking is in patients at, or after, the menopause, where a stalked fibroid gives trouble by twisting its pedicle, or by shrinking to such a size that it falls into the true pelvis and becomes impacted; or, more rarely, the pedicle of such a tumor may entangle a loop of small intestine and obstruct it.

There are two methods of removing the uterus in the radical treatment of fibroids, namely: vaginal hysterectomy and abdominal hysterectomy.

Vaginal hysterectomy is applicable only when the tumor is small or septic.

There are two methods of removing the uterus by the abdominal route: one, known as subtotal hysterectomy, in which the body and a variable portion of its neck is removed; and total hysterectomy, in which the body and neck of the uterus are completely removed.

Subtotal hysterectomy is a simpler operation than removal of the whole uterus. When carefully performed, within a few weeks of the operation the stump is movable and the vaginal vault free and undamaged, and the condition of the parts is such that by digital examination or inspection it would be difficult to determine that the patient had lost her uterus.

The disadvantages urged against this method are the liability of the stump to be attacked by cancer and the greater risk of the patient to intestinal obstruction.

Total hysterectomy is a severe procedure and attended often with more shock than the subtotal operation; it is also attended with risk of injury to the vesical segments of the ureters.

Experience teaches that subtotal hysterectomy in a spinster or childless married woman with a large fibroid in a uterus with a long narrow neck and an undilated cervical canal is as safe as any major operation in surgery.

Total hysterectomy should, as a rule, be reserved for those who have had children and in whom the cervical canal is patulous, perhaps septic and in many cases large and hard, or large and spongy. If there be the least suspicion of malignancy associated with the tumor then complete removal of the cervix with the uterus is an indispensable condition.

Fibroids of the Round Ligament of the Uterus.—This structure like the ovarian ligament, is practically a process of the muscular tissue of the uterus, and tumors in all respects like the fibromyomata of the uterus arise in this ligament, not only in the segment which lies in relation with the anterior layer of the mesometrium, but also in the terminal portion which traverses the inguinal canal. I have seen tumors of this kind as big as the fist, but their structure was rather that of a spindle-celled sarcoma than of the typical uterine fibroid. Similar tumors have been described as "desmoid," especially those connected with the inguinal portion of the round ligament.

Fibroids of the Ovarian Ligament.—It is no uncommon thing to find a fibroid the size of a cherry in the ovarian ligament, when the uterus itself is occupied by a crowd of fibroids; otherwise it is very rare to find a tumor in this process of the uterus, and especially one large enough to be obvious on clinical examination.

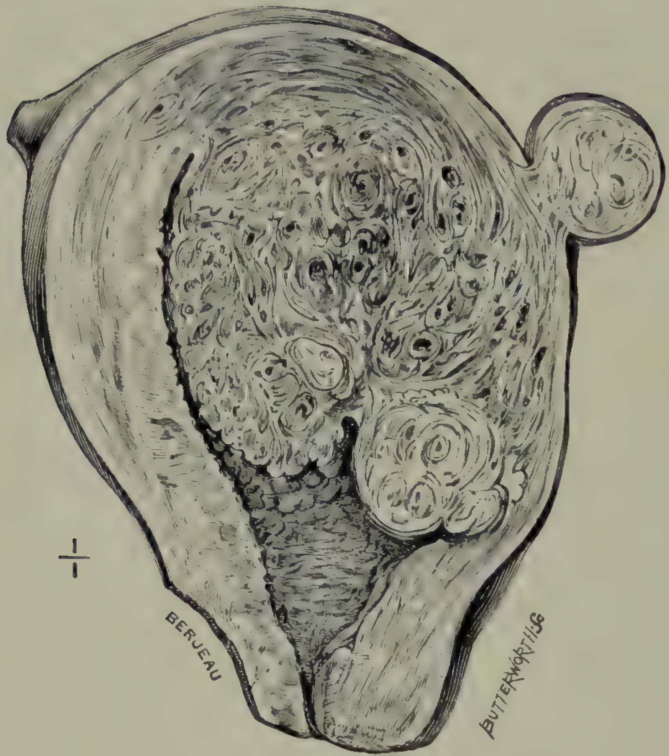

Fig. 203.—Uterus in Sagittal Section Showing Diffuse Adenomyoma from a Spinster Thirty-two Years of Age.

The gland spaces were cystic and filled with gelatinous material.

Fibroids of the Utero-sacral Ligament.—Occasionally a fibroid is found burrowing under the posterior layer of the mesometrium and simulating a primary tumor of this structure, but when enucleated it is found attached to the side of the cervix near its junction with the body of the uterus by a very narrow, tendon-like stalk. It is probable that such a fibroid arises in the tissue of the utero-sacral ligament. In three examples under my own care the fibroids had a diameter of 12 cm. Each of these was shaped like a plum and possessed a definite capsule; the true tumor tissue was myxomatous.

Adenomyoma of the Uterus (Adenomyoma uteri diffusum benignum).—The term "adenomyoma" is applied to a pathologic condition of the uterus, the leading features of which are admirably summarized by Cullen in the following terms: "It is diffuse in character, situated in the middle layer of the uterine wall and is dependent on the uterine mucosa for its glandular elements." Although several observers, including Recklinghausen, have recorded isolated examples of this disease, Cullen seems to have been the first to draw attention to its clinical importance (1897).

In well-marked cases adenomyoma presents clinical features which cause it to resemble the common varieties of submucous fibroids. The ages of the patients vary from twenty to fifty years; the uterus is enlarged, there is profuse and in some instances uncontrollable menorrhagia and profound anemia.

When the uterus is removed and divided longitudinally, the walls are seen to be greatly thickened, measuring in some specimens 5 cm. (2 inches) in thickness; this increase is due to the formation of new tissue between the outer wall of the uterus (the subserous stratum) and the superficial layer of the endometrium. There is no attempt at encapsulation, and the term "diffuse" is thoroughly justified. The new tissue consists mainly of bundles of plain muscle fiber, which instead of being arranged in vortices, as is so common in the ordinary hard fibroid, are disposed in an irregular manner, and the spaces between the bundles are filled with the peculiar stroma of the uterine mucosa containing gland tubules lined with columnar epithelium and of the same type as the normal tubular glands of the endometrium. The glandular elements appear to be uniformly distributed throughout the adventitious tissue, and can be detected up to the limits of the thin muscular stratum underlying the peritoneal coat of the uterus.

My experience of this disease is limited to three cases. In each the uterus was removed for what may, without any exaggeration, be described as uncontrollable menorrhagia, and in each it was supposed to be due to a submucous fibroid.

Ovarian Fibroids.—Solid ovarian tumors have puzzled pathologists and surgeons on account of the great difficulty of detecting specific differences in their minute structure even with all the resources of histologic chemistry which would enable distinctions to be made between the harmless fibroid, a spindle-cell sarcoma, and a fibroid.

Attention has been drawn to the importance of encapsulation as a feature indicating innocence (p. 737); this can be relied on in determining between a fibroid and a malignant tumor of the ovary.

In their most typic form ovarian fibroids present easily recognizable characters. They are ovoid and of regular contour, quite smooth, intensely hard, and, as a rule, free from adhesions and unilateral. I have seen both ovaries affected in this way in one instance only. One pole of the tumor is connected with the ovarian ligament, and if the tumor be bisected in such a way as to include this ligament, a small portion of the normal ovary, amounting in a large fibroid to an infinitesimal portion of the whole tumor mass, will usually be detected associated with the ligament. For example, the specimen represented in Fig. 204 is drawn of natural size, and the remnant of ovary does not offer any great disparity when compared with the mass of the fibroid, but when the tumor weighs several pounds the small, bud-like piece of ovary appears very incongruous. A little attention to this relation of tumor, remnant of ovary, and ovarian ligament is of importance, as it affords an extremely simple means of recognition. When the tumor is bisected the cut surface displays the peculiar whorled disposition which is so distinctive of the hard uterine fibroid, and it agrees with this species of tumor not only in its microscopic characters, but also in being encapsuled. In small tumors as well as in those of moderate size it is easy to demonstrate the capsule on any part of its surface; even in very large examples, in which the capsule has become extremely thin in the parts about the outer pole of the tumor, it is usually quite easily demonstrable around the inner or uterine pole. Fairbairn is careful to point out that although in the typic forms of ovarian fibroid the tumor arises within, and in the majority of cases remains restricted to, and actually encapsuled in the ovary, no matter what size it attains, yet there are examples which grow within the ovary and project from its surface like subserous fibroids of the uterus. This may be true, and it is probable that some tumors known as corpora fibrosa (Patenko), supposed to arise from corpora lutea, are of this nature.

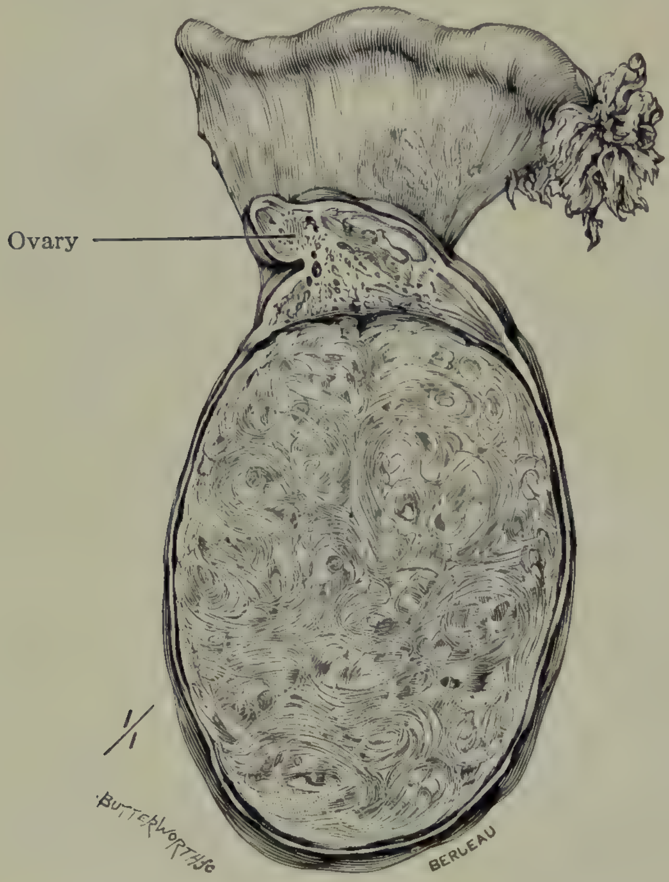

Fig. 204.—Ovarian Fibroid in Section (Natural Size). From a woman thirty years of age.

However much ovarian fibroids may resemble uterine fibroids in possessing definite capsules, and in their gross as well as minute structure, and the vortex-like arrangement of the constituent tissues, they differ in a very marked way in their age-distribution. Uterine fibroids only arise during menstrual life, which in its widest sense gives them an age limit of thirty years (fifteen to forty-five), but ovarian fibroids arise in advanced life. Fibroids of the uterus and the ovary occasionally coexist.

Ovarian fibroids sometimes soften, and this leads to the formation of spurious cysts in their substance. Another feature of some importance, and one already mentioned, is their intense hardness; and in some cases this is so obvious that it has enabled me to suspect the nature of the tumor before operation. Calcification has been observed in them, but this is rare; and they are occasionally complicated with hydroperitoneum, and, except in this circumstance, they rarely produce any obvious impairment of the general health.

Tumors of the ovary described as myomata will require reinvestigation in the light of this additional knowledge; for the present they may be safely included in the same species.

One of the greatest difficulties in connection with our knowledge of the solid tumors of the ovary, especially the variety termed fibroma, has been the absence of information concerning the after-history of cases in which patients have been submitted to operation. This defect has been removed by the publications of Doran, Briggs, and Fairbairn.

I have followed up the after-history of ten cases under my own care. Nine were alive at intervals varying from one to six years after operation. One case died from a chronic affection of the lung and pleura.

Baillie (1799) gives a good figure of an ovarian fibroid and writes that "it resembles exactly in its texture" uterine fibroids and draws attention to its rarity.

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Baillie: "The Morbid Anatomy of the Human Body," London, 1799. Plate VII.
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Myomata, or tumors composed of unstriped muscle fiber, are very rare, and are met with exclusively in organs containing this tissue, *e. g.*, the esophagus, stomach, duodenum, bladder, and uterus.

Attention has already been directed to the difficulty of determining between the fusiform cells of sarcomata and unstriped muscle fiber. This difficulty is further increased by the fact that many malignant tumors composed of spindle cells (sarcomata) contain tracts of cells which present a transverse striation such as is seen in voluntary muscle in its embryonic stage; but it is remarkable that cells with the transverse striation occur in situations where voluntary muscle is not found normally. It is also a fact that tumors consisting of mature striated (voluntary) muscle fiber have not been observed. Much caution needs to be exercised before deciding that a tumor is a myoma; formerly many of the spindle-celled sarcomata of the choroid were regarded as myomata arising in the ciliary muscle. It is also extremely probable that many of the tumors described as myomata from the esophagus, stomach, duodenum, bladder, vagina, and skin were sarcomata. The common situation for tumors containing unstriped muscle fibers is the uterus (see Fibroids, p. 771).

Myxomata.—These are tumors composed of tissue identical with the jelly-like substance which exists in the umbilical cord. Here we have to deal with a difficulty, because there is a very great tendency in many connective-tissue tumors to degenerate into this soft gelatinous or myxomatous tissue and become as diffluent as the vitreous body in the eyeball.

The common nasal polypus furnishes an excellent example of this tissue; it consists of cells with long, slender processes interlacing with those of adjacent cells and ramifying in a structureless, unstainable, diffluent mass, the whole being bounded by a thin layer of mucous membrane covered with columnar ciliated epithelium. Nasal polypi may be regarded as pendulous processes of edematous mucous membrane.

The condition termed an aural polypus has no claim to rank as a tumor; it consists of myxomatous tissue. Jacobson has suggested that tympanic polypi consisting of myxomatous tissue may arise in vestiges of the fetal connective tissue which fills the tympanum at birth and slowly disappears as pulmonary respiration is established.

The tumors which have come under my notice and to which the term myxoma most properly applies have grown from the lumbar fascia; they were sessile tumors, and when cut open looked like colorless masses of transparent trembling jelly. These tumors recurred after removal; in one case there were several recurrences extending over a period of ten years. There was no evidence of dissemination. It is probable that they were sarcomata which had undergone myxomatous degeneration. It would be convenient and perfectly justifiable to deprive myxomata of even the rank of species among tumors.

The heart is, of all the organs of the body, the least liable to tumors, primary or secondary, yet the few examples of primary tumors which have been observed in it are described by the reporters as fibromata, or myxomata, or fibromyxomata. The chief cases have been collected and the clinical signs analyzed by Pavlowsky.*

GROUP II.—TUMOR-DISEASES OF THE TEETH.

Odontomata.—An odontoma is a tumor composed of dental tissues in varying proportions and different degrees of development, arising from teeth-germs or teeth still in the process of growth.

In a developing tooth three distinct elements have to be considered: the enamel-organ, derived from the buccal epithelium; the papilla, from which the dentine is derived; and the tooth-sac, which furnishes the cementum. At an early stage in its development the various tissues concerned in the development of the hard parts of a tooth are quite soft and, enveloped in a sac, lie buried in the soft tissues covering the dental borders of the jaws. Odontomes may be produced by aberrations of any or all of the embryonic parts concerned in the production of a tooth and at any stage of its development.

Epithelial Odontomata.—It is well known that encapsuled tumors of a peculiar type occur in connection with the alveolar borders of the mandible, but more rarely in the maxilla, which display on section a congeries of cysts varying in size and shape. These loculi contain brown mucoid fluid and the septa between them are sometimes ossified. The growing portions of these tumors have a reddish tint not unlike a myeloma. Microscopically the solid parts consist of branching and anastomosing columns of epithelium, portions of which form alveoli. The cells lining these alveoli vary, the outer layer may be columnar while the central cells degenerate and resemble the tissue of the stellate reticulum of the enamel-organ. These tumors, which are most common about the twentieth year of life, but are occasionally met with much later, were investigated by Eve and labeled by him "multilocular cystic epithelial tumors of the jaw," and he followed Falkson and Bryck in attributing their origin to persistent epithelial remnants of the enamel-organ. I accepted this line of argument and satisfied myself that epithelial remnants of this character are demonstrable, but a careful re-examination of a few specimens and a study of the description of others, especially those which arise in individuals past middle life, has satisfied me that many of these supposed epithelial odontomata (multilocular cystic epithelial tumors of the jaws) exhibit local malignancy and are endotheliomata arising in the gums.

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* "Berlin. klin. Woch.," 1895, S. 393.

Follicular Odontomata.—Under this heading are comprised the tumors formerly called dentigerous cysts, a term which came to be used so loosely that it was discarded in the necessity for precision.

In its typical form a follicular odontoma consists of a tough fibrous sac of varying thickness, which represents the tooth-sac or follicle. In some specimens the sac is thin and crepitant, in others it may be more than a centimeter thick with ossific trabeculæ. The cavity of the sac usually contains viscid fluid and the crown or the root of an imperfectly developed tooth. Exceptionally the tooth is absent or represented by an ill-shaped denticle. The tooth is sometimes inverted, and even when the crown is of good shape the root is truncated.

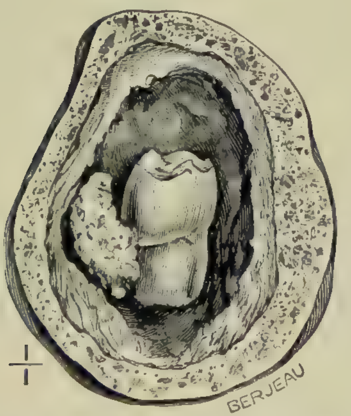

Fig. 205.—A Follicular Odontoma from the Right Half of the Mandible of a Boy Aged Fourteen Years.

Removed by Wormald, 1850. (Museum Royal College of Surgeons.)

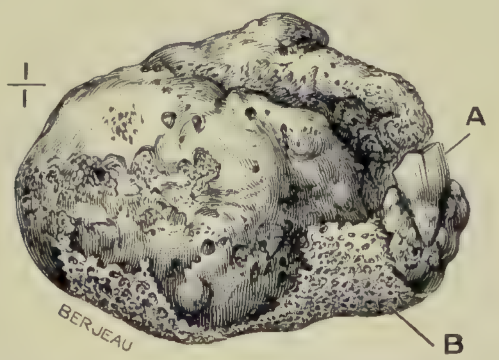

Fig. 206.—An Odontoma from the Mandible of a Rickety Youth aged Nineteen Years.

A, Denticle; B, portion of the outer wall of the jaw.

Follicular odontomata arise in connection with the permanent teeth, especially the molars; they sometimes attain very large proportions, especially when they arise in the upper jaw, and if they should happen to be bilateral, produce hideous deformity.

Fibrous Odontomata.—In a developing tooth a portion of the connective tissue in which it is embedded is found to be denser and more vascular than the rest; it also presents a fibrillar arrangement. This condensed tissue is known as the tooth-sac, and when fully developed presents an outer firm wall and an inner looser layer of tissue. At the root of the tooth the follicle-wall blends with the dentine papilla, and is indistinguishable from it. Before the tooth cuts the gum it is completely enclosed within this capsule. Under certain conditions this capsule becomes greatly increased in thickness, and so thoroughly encysts the tooth that it is never erupted. Such thickened capsules are mistaken for fibrous tumors, especially if the tooth be small and ill-developed. Under the microscope they present a laminated appearance, with strata of calcareous matter. To these, the term fibrous odontomes may be applied. They are more common in ruminants than in other mammals, and are especially frequent in goats. As a rule, they are multiple, four being by no means an unusual number. They occur in marsupials, bears and lions, as well as in man.

There is good reason to believe that rickets is responsible for some of these thickened dental sacs. Some of the most typical examples that have come under my observation occurred in rickety children. Severe operations have in some instances been performed under the impression that the tumors were sarcomata, even when bilateral.

Cementomata.—When the capsule of a tooth becomes enlarged, as in the specimens just considered, and these thick capsules ossify, the tooth will become embedded in a mass of cementum. To this form of odontoma the name cementoma may be applied. Odontomata of this character occur most frequently in horses, and sometimes attain a large size. The tumor which most nearly approaches a cementoma in the human subject that has come under my notice is represented in Fig. 206. This patient was under the care of Mr. W. A. Maggs, of Guy's Hospital. This tumor occupied the position of the first right lower molar, and a rudimentary representative of the tooth is shown in the drawing. The lad had had rickets.

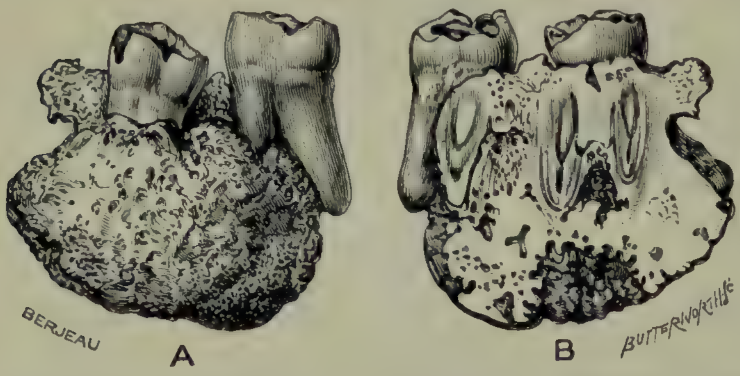

FIG. 207.—AN OSSIFIC BALL IN WHICH ARE EMBEDDED THE TEETH OF TWO LOWER MOLARS.
A, The tumor entire; B, in section.

Compound Follicular Odontomata.—If the thickened capsule ossifies sporadically instead of uniformly, a curious condition is brought about, for the tumor will then contain a number of small fragments of cementum, or dentine, or even ill-shaped teeth (denticles) composed of three dental elements—cementum, dentine, and enamel. The number of teeth and denticles in such tumors varies from fifteen to forty. Remarkable cases of this kind have been recorded by Tellander, Tomes, Windle, and Hildebrand among others.

Radicular Odontomata.—This term is applied to tumors which arise after the crown of the tooth has been completed, and while the roots are in the process of formation. As the crown of the tooth, when once formed, is unalterable, it naturally follows that should the root develop an odontoma, enamel cannot enter into its composition; the tumor would consist of dentine and cementum in varying proportions, these two tissues being the result of the activity of the papilla.

There are reasons for believing that some swellings connected with the roots of teeth resembling radicular odontomata are of inflammatory origin. The rounded swelling enveloping the roots of two molars (Fig. 207) is an example of this, and the microscopic examination of the tumor supports this view. The roots of the molars are embedded in an ossific ball and do not mingle with its tissue. The teeth were removed by Mr. Murray from the mandible of a youth aged twenty-one years in whom it had been noticed several years. One of the molars has a carious crown.

An odontoma as remarkable as this is represented in Fig. 208. It was extracted "with no little difficulty" from a Chinese student aged nineteen years by Dr. Davenport. This tooth caused no trouble until two months before it was extracted. There was a swelling around the tooth supposed to be due to an abscess. At first sight the lump on the root of the tooth looks like a radicular odontoma, but on section it has the appearance and structure of a composite odontoma. The clinical report contains the significant statement that there were no signs of the lower wisdom teeth.

Composite Odontomata.—This is a convenient term to apply to those hard-tooth tumors which bear little or no resemblance in shape to teeth, but occur in the jaws, and consist of a disordered conglomeration of enamel, dentine, and cementum. Such tumors may be considered as arising from an abnormal growth of all the elements of a tooth-germ—enamel-organ, papilla, and follicle.

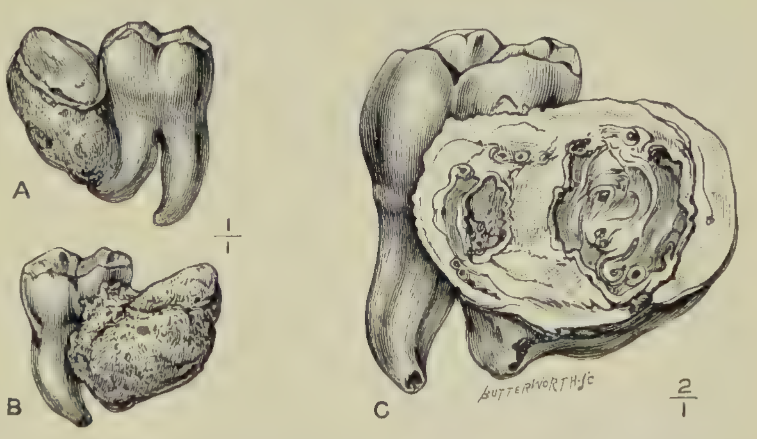

FIG. 208.—THE SECOND RIGHT MANDIBULAR MOLAR OF A CHINAMAN AGED NINETEEN YEARS WITH A SWELLING POSSESSING THE CHARACTERS OF A COMPOSITE ODONTOMA.

A and B, Tooth natural size; C, enlarged and in section.

Not only is this set of odontomata composite in that the tumors comprised in it originate from all the elements of a tooth-germ, but they are composite in another sense. In the majority of cases the tumors are composed of two or more tooth-germs indiscriminately fused. But they differ from the cementomata containing two or more teeth in the fact that the various parts of the teeth composing the mass are indistinguishably mixed, whereas the individual teeth implicated in a cementoma can be clearly defined.

On looking over a long series of composite odontomata it is curious to find how greatly they differ in shape. For example, the tumor Fig. 209 in no way recalls the shape of a tooth, yet the whole of its convex surface (for it is shell-shaped) is covered with well-marked cusp-like processes of enamel.

Composite odontomata attain a larger size in the upper than in the lower jaw. The tumor Fig. 210 is the largest odontoma from the mandible I have seen; it weighs 885 grains.

Dental Cysts.—It occasionally happens in extracting dead permanent teeth that a small fibrous bag is found at the apex of the root, often no larger than an apple pip, though sometimes it may be as big as a bantam's egg, filled with fluid, and often containing crystals of cholesterin. These sacs or dental cysts occur in connection with the dead roots of mandibular and maxillary teeth; they sometimes attain a large size in the upper jaw when they invade the antrum, and some of these cysts are of sufficient size to simulate an abscess of that cavity.

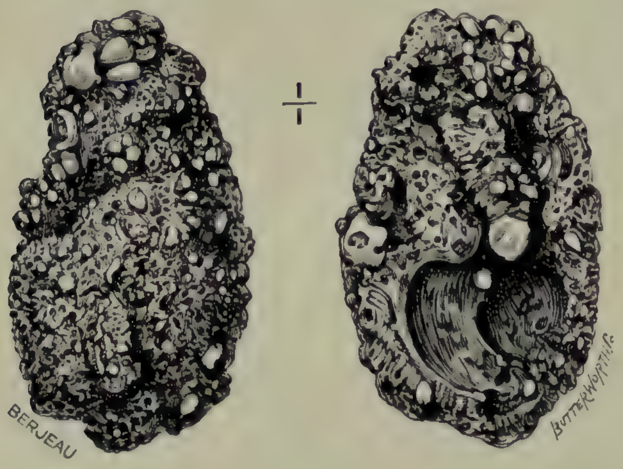

Fig. 209.—A Composite Odontoma from the Mandible.

The patient, an inmate of a workhouse, had been troubled with it many years; one day she felt it loose in her mouth and "spat it out."

The constant association of these cysts with the dead roots of permanent teeth has led many observers to regard them as pus sacs with thick fibrous walls. J. G. Turner has carefully investigated their structure and demonstrated the existence of an epithelial lining in many of these cysts. He believes that they arise in the "rests" detected by Malassez and known as para-dental epithelial remnants. They are derived originally from a prolongation of the enamel organ which precedes and determines the formation and shape of the dentine and the root of the tooth.

The restriction of these cysts to the roots of the permanent teeth is explained by the fact that the roots of temporary teeth as well as their alveoli are absorbed.

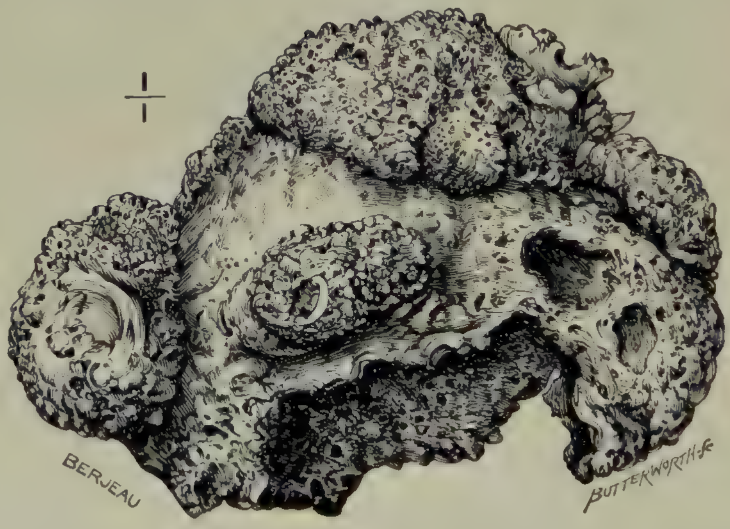

Fig. 210.—A Composite Odontoma from the Mandible of a Boy Fourteen Years of Age.

Removed by Mr. Brothers with an elevator (Museum Royal Dental Hospital, London.)

The majority of dental cysts are met with accidentally in extracting dead permanent teeth or their roots. Large specimens, however, resemble in their clinical signs tumors of the jaws or antrum. When a painless smooth tumor of the jaw is associated with a chronic carious tooth, a dental cyst should be borne in mind.

Clinical Characters.—The germ of any permanent tooth may develop into an odontoma, and occasionally two or more teeth may be involved in the one tumor. Odontomata occur with equal frequency in the upper and lower jaws, and the follicular species is very apt to be multiple, and four have been found concurrently in the jaws of the same patient. The composite species ranks next in frequency with follicular odontomata, and in the upper jaw an odontoma may invade the antrum and attain the size of a child's fist. In the mandible they rarely exceed a dove's egg in size, but the specimen represented in Fig. 210 shows that in this situation an odontoma may attain a good size.

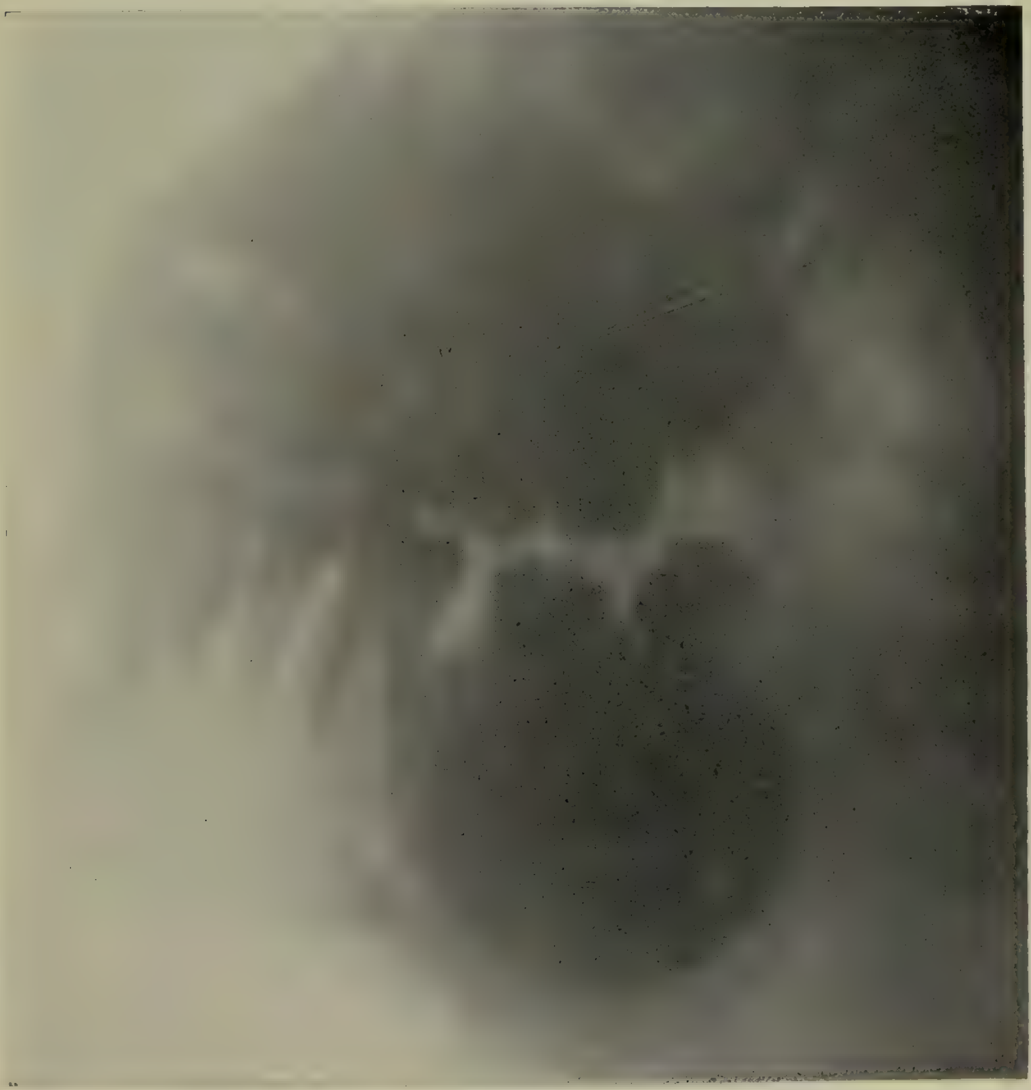

Fig. 211.—Skiagram of an Odontoma in the Mandible of a Boy Aged Fifteen Years.

There is a clinical point in the natural history of odontomata of some importance. A careful examination of the clinical history shows that in nearly all cases the tumor has remained quiescent, and then there comes a period in which, like a tooth, it seems to erupt and make its way above the gum and cause very often profound constitutional disturbance, mainly of a septic character. In some of reported cases it is stated that the patients have been so ill as to be near death. This phenomenon usually happens between the twentieth and the twenty-fifth years. In a fair number of cases relief has come to the patient and the illness has ended by the odontoma loosening spontaneously. In several instances it is said that the patient "spat it out." This happened with the specimen Fig. 209. One of the largest odontomata known, after producing hideous deformity of the face and sloughing of the cheek, fell out of its own accord. The large odontoma Fig. 210 caused the boy so little inconvenience that he ran about a village with part of the tumor sticking out of his mouth till Mr. Brothers, Cape Town, removed it with a strong elevator.

The diagnosis of these tumors has been a matter of great difficulty in the past. In many the swelling has been regarded as a myeloma, or a sarcoma, but in the majority of cases, especially where there has been free suppuration around the odontoma, it has been regarded as a sequestrated piece of dead bone. The x-rays have proved serviceable in enabling a correct diagnosis to be made.

Treatment.—A study of the literature relating to the treatment of odontomata is very instructive, because it reveals that operations unnecessarily severe have been undertaken in ignorance of the nature of the disease by surgeons of high reputation and wide experience. In several instances it is known that a great portion of the mandible has been excised under the impression that the tumor was malignant in nature. In some very large odontomata of the upper jaw the tumor has been removed without an anesthetic, the procedure being described, in the words of the operator, as "a surgical struggle" (Duka, Michon). In some of the cases dentists succeeded in removing the odontoma with forceps, thinking that they were dealing with unerupted (buried) teeth. In others the nature of the tumor has been suspected and in the course of its excision the mandible has been broken and remained permanently ununited.

In the case of a tumor of the jaw, the nature of which is doubtful, particularly in a young adult, it is incumbent on the surgeon to satisfy himself, by the use of the x-rays, before proceeding to excise a portion of the mandible or maxilla, that the tumor is not an odontoma, for this kind of tumor only requires enucleation. In the case of a follicular odontoma it is usually sufficient to excise a portion of its wall, scrape out the cavity, remove the tooth if one be present, stuff the sac, and allow it to close by the process of granulation.

GROUP III.—EPITHELIAL TUMORS.

Papillomata (Warts).—A papilloma consists of an axis of fibrous tissue containing blood-vessels surmounted by epithelium projecting from an epithelium-covered surface; it may be simple and present a uniform surface, or be covered with secondary processes and resemble a mulberry.

Warts growing from surfaces covered with squamous epithelium are, as a rule, hard; for example, those which grow on the skin and in the larynx. When they grow from mucous membrane they are soft, and in some situations the axis, or core, of the papilloma is formed of loose connective tissue. Such are known as villous papillomata and are common in the bladder.

On the skin warts occur singly or in multiple. Occasionally they are crowded on a restricted area of the skin and form a wart-field. Warts are rarely painful unless irritated; then they are apt to ulcerate and bleed. Crops of warts are common on the hands of children, and in adults in the region of the anus, vulva, and glans penis when these parts are irritated by foul discharges, especially those of gonorrheal origin. A curious feature of multiple warts is that they sometimes appear on the hands or scalp almost suddenly, and after persisting many weeks, or perhaps months, disappear as if by magic. When warts are thickly crowded upon a limited area of skin—such, for example, as the glans penis—they are apt to be mistaken for more serious disease, such as warty carcinoma. When soft warts appear in great number near a mucocutaneous orifice they are due to local infection by microörganisms.

Skin warts are overgrown papillæ, and on section the epithelium will be found to pass from one papilla to another in an unbroken line without invading the fibrous framework.

A solitary wart may occur on any skin-covered surface and persist. A wart of this character sometimes attains the size of a walnut, and in some cases is mottled with black pigment. Such warts, late in life, may become the starting-points of melanomata (see p. 756).

Solitary warts sometimes grow rapidly, and become so large that they are apt to be mistaken for malignant tumors. They are red, like the comb of a cock, and are smeared with purulent material, and sometimes become abominably fetid. Billroth drew attention to large, rapidly growing tumors of this kind which arose in soft warts of the face, and termed them plexiform sarcomata.

Warts growing from the skin are covered with squamous epithelium, and the surface cells are liable to be transformed into horny material, and form what are called cutaneous horns. Some of these wart-horns have attained almost fabulous dimensions.

Laryngeal Warts.—(See chapter on Diseases of the Larynx.)

Intracystic Papillomata.—All true cysts are lined with epithelium, and this is often the source of cysts. The most common varieties of papillomatous cysts arise in the mammary gland and in the hilum of the ovary. In the former the best marked examples arise in those cysts which are due to the abnormal dilatation of galactophorous ducts. The large papillomatous cysts of the ovary probably arise in the epithelial remnants of the mesonephros (see p. 846). A much rarer form of wart-bearing cyst is that which arises from the dilatation of the duct of a sweat gland.

Villous papillomata grow from the mucous membrane of the bladder and the lining of the renal pelvis, and the choroid plexuses of the brain.

In the bladder the villi have the appearance of long, branching, feathery tufts which recall the delicate chorionic villi, and when viewed in the living bladder by means of the cystoscope are exquisite objects. Both in the bladder and the kidney villous papillomata give rise to frequently recurring hemorrhages imperilling life.

The choroid plexuses of the ventricles occasionally greatly enlarge and give rise to unpleasant effects. In some instances, when this happens to the choroid plexus of the fourth ventricle, the mass will press upon the vital structures in the floor of that cavity and destroy life.

Adenomata.—These are tumors constructed upon the type of and growing in connection with a secreting gland. Adenomata occur as encapsuled tumors in such organs as the mamma, liver, the parotid and thyroid glands; when they arise in connection with the intestine, rectum, or uterus they form pedunculated more or less globular processes often known as polypi. A single adenoma may exist in a gland, but often there is more than one. In size they vary greatly; some are no bigger than peas, whereas an adenoma in the mamma or the thyroid gland may form a mass as big as a man's head.

Adenomata contain glandular spaces, and though they do not furnish the secretion peculiar to the gland in which they arise, they nevertheless produce in many instances a perverted secretion which leads to great distention of the spaces in the tumor and converts it into a cystic body. Tumors of this kind in the mammary gland are sometimes called adenoceles, and in the thyroid body bronchoceles. The epithelium lining the cyst walls of adenoceles often contains soft papillary processes; these are known as intracystic papillomata. They occur, though rarely, in bronchoceles.

Very large tumors made up of large cavities lined with epithelium are common in the ovary; these are sometimes called adenomata. They will be described with dermoids and embryomata.

The effects of adenomata depend upon their size and situation. A large mammary adenoma may be painless, but the disfigurement it causes will annoy the patient. The small, hard fibro-adenomata are often associated with painful sensations in the mamma.

In the thyroid gland a bronchocele may be so big that the patient has to support it in order to walk about, and yet it neither endangers life nor produces pain; but a solid adenoma of this gland lying close to the trachea will so compress this tube as to bring about fatal dyspnea.

The following statements hold for all adenomata: When completely removed they do not recur; they do not infect lymph glands nor give rise to secondary deposits.

Cause.—A study of the probable mode of origin of adenomata is interesting. The prevailing view as to their origin is that they arise from "rests" or small pieces of gland tissue accidentally detached in the process of development from the main gland. This mode of origin may hold for the fibro-adenomata so common in the mammæ of young women, but it is an unsatisfactory explanation of the larger and cystic forms met with in older women. It is well known that the irritation of gland-epithelium by microörganisms and particular protozoa will excite it to multiply, an effect easily observed in the bile-ducts of rabbits infected by coccidia. It has also been shown that the well-known enlargements of the prostate after middle life are probably due to infective agents which gain access to the gland recesses from the urethra and set up chronic inflammatory changes. If this method of causation can be established for the prostate, it will help us to understand the mode of origin of many so-called adenomata of the mamma, namely, those that are to be regarded as the sequence of catarrhal changes affecting the excretory ducts of the gland. The bearing of these views on the causation of cancer is very great, because it has been emphasized by many writers, and indeed it is a matter of common observation, that cancer is much more prone to arise in organs the seat of chronic inflammatory changes than in those thoroughly healthy.

It cannot be too strongly affirmed that adenoma and cancer may coexist in the same gland, but there is absolutely no evidence to show that an adenoma changes its character and becomes malignant. However, in discussing the nature of cancer I will attempt to show that cases not infrequently come to hand in which it is impossible to decide from a microscopic examination whether a given tumor should be called an adenoma or a cancer.

Treatment.—Adenomata should be removed whenever possible; in the case of the mammary and the thyroid glands this proceeding is one of the simplest and safest in surgery.

Carcinoma (Cancer).—This term in the strict sense in which it is used by pathologists signifies a malignant tumor arising in epithelium. The disease is one of very great importance on account of its insidious onset, and, in its earliest stages, its painlessness; the ignorance which prevails regarding its cause; its progressive and irresistible destructiveness; the manner in which it infects lymph glands; the extraordinary effects it produces in different organs on account of the dissemination of the growth in the form of secondary nodules; the hopelessness, misery, and pain it produces when fully developed; and the inability of medical and surgical art to deal effectively with it, save in its very earliest stages. Although this disease was recognized in the earliest dawn of medicine, yet we remain ignorant of its cause; indeed, in many instances the diagnosis of this malady is often uncertain in the living and the source of many errors even among men of great experience and reputation. This is not due to supineness on the part of investigators, but to the absence of what has been called "specific symptomatology."

Varieties of Cancer.—Epithelium plays two great parts in the animal economy: *protective*, as in the skin, and *secretory*, where it is found in glands. When carcinoma arises from surfaces covered with epithelium of the protective variety it is called squamous-cell cancer, and when it arises in the epithelium of glands it is termed glandular cancer.

The microscopic structure of a carcinoma is very simple, and consists of columns of cells, so that when the columns are cut at right angles the section has the appearance of a number of alveolar spaces filled with epithelium. The walls of these alveoli are composed of fibrous tissue, presenting various degrees of density, in which blood and lymph vessels ramify. These cell-columns are not always simple, but may branch in various directions and thus produce in some sections very complicated appearances, the softness or hardness of the cancer depending on the amount of fibrous tissue between the columns of cells. This plan of structure underlies all the varieties of malignant epithelial tumors, even those which arise on surfaces covered with squamous epithelium. The cells composing the columns depend upon the character of the epithelium in which the cancer originates, and this feature is so striking that the histologist can often pronounce with certainty the particular gland in which a cancer arose, merely from studying a carefully prepared specimen under the microscope.

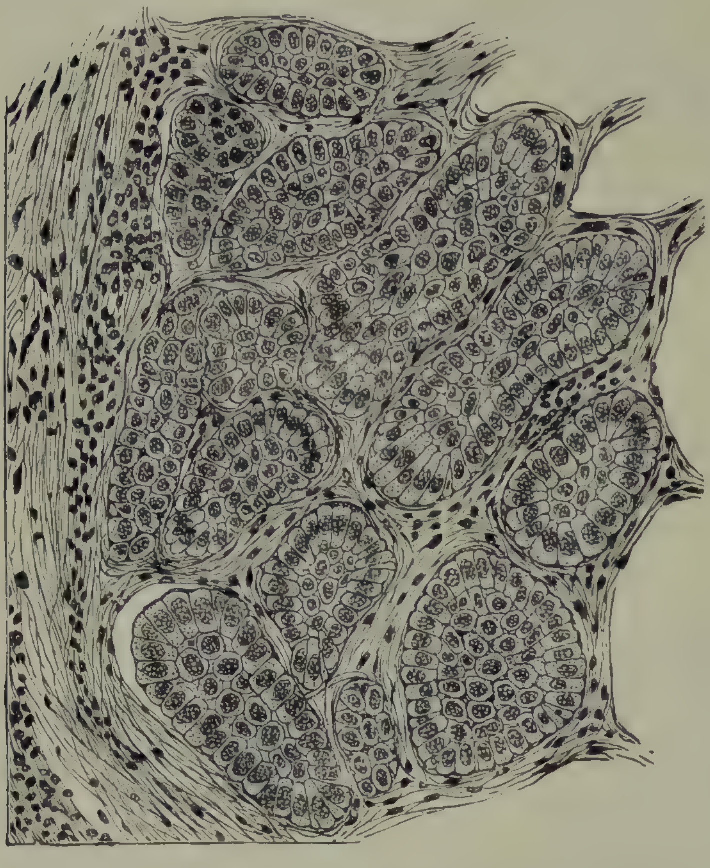

FIG. 212.—MICROSCOPIC APPEARANCE OF CANCER ARISING IN THE NECK OF THE UTERUS. (From "Diseases of Women," Bland-Sutton and Giles.)

Stroma and Parenchyma.—Every tumor, whether it be a lipoma or a rapidly growing sarcoma, presents a stroma and a parenchyma. These two elements are particularly observable in adenomata and carcinomata on account of the striking difference in the character of the connective tissue and the epithelium. In the case of carcinoma, as the epithelial cells multiply and intrude into the adjacent tissue, the intrusion is answered by a formation of fibrous tissue; this response is less marked in rapidly growing tumors than in those which grow slowly. This response of the tissues to irritation has been termed the "specific tissue reaction," but it is as obvious in many of the common forms of tissue irritants, such as microörganisms, and especially foreign bodies. In the case of sarcomata a kind of investment is furnished for each cell, but in carcinomata for groups of cells, producing in reality a fibrous tissue maze.

Squamous-cell Cancer.—This may make its appearance on any surface covered with stratified epithelium. It may arise as a wart-like growth, more frequently as a small circular ulcer with raised, rampart-like edges, or as a fissure, and it is particularly apt to arise on the scrotum of the chimney-sweep. "Sweep's cancer" usually begins as a wart, which is familiarly known as a "soot-wart." A similar form of the disease is described as arising in men who work in tar and paraffin.

The common situations in which squamous-celled cancer arises are the lips, tongue, cheek, vulva, anus, scrotum, and glans penis; it occurs on the conjunctiva, pinna, urethra, at the edges of scars and chronic ulcers, and in lupus-scars. In many of these situations it is preceded by lesions, or what are sometimes called *pre-cancerous conditions*, which need consideration. Pre-cancerous is a term applied to certain local conditions which clinical observation has shown to precede cancer. Of these, the best example is the condition of the tongue known as leukoplakia, or lingual ichthyosis, and it is an observation of some interest that a condition of the labia majora identical with leukoplakia as seen on the tongue and buccal mucous membrane is a forerunner of cancer of those structures. It is also established that chronic ulcers of the skin, the esophagus, the stomach, and lupus-ulcers, and especially chronic syphilitic ulcer of the tongue, become the seats of cancer.

It has been long recognized that cancer of the neck of the uterus is much more common in women who have borne children than in barren women, and my own observations fix it as high as 95 per cent.; it is undeniable that the more children a woman bears, the greater is her liability to this form of cancer. This is due to traumatism of the cervix uteri connected with childbirth. A very significant feature in connection with the liability of organs to become cancerous is the well-known fact that a diseased mamma, uterus, thyroid gland, tongue, or gall-bladder is much more prone to become the seat of cancer than one which is healthy.

In regard to goiter as a pre-cancerous condition, it is worth mention that malignant disease of the thyroid gland is very common in districts where goiter is endemic, and an excessively rare affection in countries where goiter occurs sporadically.

The gall-bladder is another organ of interest in relation to pre-cancerous conditions, for it is exceptional to find a cancerous gall-bladder without finding gall-stones associated with it. Some writers assume that the concretions are the cause of the cancer. This is difficult to prove. Others suggest, and with more reason, that the chronic inflammatory changes which are so often found in gall-bladders occupied with concretions are favoring or predisposing conditions for the development of cancer. It is noteworthy that primary carcinoma of the gall-bladder is three times more common in women than in men, and the evidence indicates that if gall-stones do not actually predispose to or cause cancer of the gall-bladder, there are some closely allied conditions favorable to the occurrence of each.

The ulcer which indicates the beginning of a squamous-cell cancer, when left to follow its own course, may extend and involve extensive tracts of tissue, or fungate and form large granulating dendritic masses. In both cases the superficial parts are continually cast off in a foul fetid discharge containing sloughs of tissue, cellular detritus, and blood. Vascular tissues, such as skin, muscle, and mucous membrane, are quickly infiltrated and destroyed; even bone is rapidly eroded. Cartilage resists invasion; this is seen in a striking way in those rare instances where cancer attacks the pinna; the skin and soft tissues quickly disappear, while its cartilaginous framework stands prominently out amidst the surrounding ruin.

In whatever situation squamous-celled cancer occurs, it destroys life rapidly. The quickness with which it ulcerates and overcomes all resistance enables it to open large blood-vessels should any lie in its way. Hence death from hemorrhage is frequent; when the cancer is near the air-passages, foul material is inspired and initiates septic pneumonia.

Carcinomata of the bladder, uterus, vagina, labia, and anus usually induce death not from their toxic effects, but from the hindrance they offer to the escape of urine, or by actually invading the walls of the bladder and ureter, which leads to infection and decomposition of the urine. Apart from the local misery, these conditions produce serious disorganization of the kidneys, and death is caused in a fair proportion of these cases by uremia.

Gland Cancer.—This variety arises in the epithelium of secreting glands; it is exceedingly common in some glands and rare in others; but the general features of this disease are the same in whatever gland it arises.

A striking feature of cancer is the fact that the primary lesion is not circumscribed. When examined clinically it is rarely possible to define the limits between the tumor and the surrounding tissues, and this indefiniteness is more obvious when, in the course of an operation, the surgeon cuts into it; but, what is more significant, when the periphery of a cancer is subjected to microscopic scrutiny, the searching eye of a competent pathologic histologist is unable to discern with accuracy the limitation of the cancerous territory.

This illimitation of cancer constitutes one of the greatest difficulties in dealing with it surgically, for it is clear, if with the aid of a microscope there is difficulty in defining its limits, how uncertain the surgeon must be in determining its extent with only fingers and eyes to guide him during an operation. This has led to the practice in recent years of complete extirpation, whenever possible, of cancerous organs. Although a cancer is for a time limited to the gland in which it arises, we have no means of distinguishing with any reasonable certainty, when the individual comes under observation, that the cancer is limited to the gland, for its outrunners quickly involve surrounding structures, whether they be skin, fat, mucous membrane, muscle, or bone. When adjacent parts are infiltrated in this way it is convenient to describe them as being implicated in the cancer. This implication of organs is a grave feature and a common cause of death, and is often a bar to operative intervention.

The insidious nature of this tissue-infiltration which is one of the dangerous features of carcinoma has recently been studied by Handley, and he has shown how a cancer of the breast, if the patient live long enough, may permeate the deep fascia throughout the whole of the body. Although cancers, like all epithelial structures, are in free communication with the lymph system, they are poorly supplied with blood; this leads to retrograde changes which it is customary to describe as degeneration.

The commonest of these changes is known as colloid degeneration, in which the epithelium in the cell-columns becomes changed into a structureless material resembling jelly; this change is particularly common in cancer of the stomach and breast. It is well known that a primary cancerous lesion may undergo retrogressive changes and almost disappear. The variety known as "withering-cancer" or "atrophic cancer" of the breast is an example of this. Patients with this kind of cancer have lived ten, fifteen, and even twenty years. The not uncommon form of cancer found in the colon, especially in the sigmoid flexure, where the growth encircles and narrows the gut so tightly that it seems as if a piece of cord were tied around it, is really a primary carcinoma undergoing spontaneous cure; but it surely destroys life, if not from its mechanical effect in obstructing the colon, by infecting the liver and peritoneum. Thus cancer manifests itself differently in the same organ and its effects vary more widely in diverse organs; for example, primary cancer of the liver is always massive and leads sometimes to enormous enlargement of this organ; it may even treble its bulk. This is also true of secondary deposits in the liver, for they attain a greater size in its tissues than elsewhere. Hillier suggests that, in addition to the large size of the liver, its small proportion of connective tissue, its blood-supply, copious and rich with food products, may explain this; carcinomatous growths contain a large amount of glycogen, and its presence in the liver may have something to do with the way in which cancer flourishes in the liver.

Primary cancer of the pancreas seldom forms a large mass, and usually appears in the head of the gland as an ill-defined swelling. The difference in the proportion of fibrous tissue in the liver and in the pancreas may offer some explanation of the variation of the size in the cancerous mass in the two organs. Cancer of the pancreas nearly always attacks the head of the gland and is excessively rare in its body or tail.

Infection of Lymph Glands.—The surfaces of our bodies, whether skin or mucous membrane, are rich in lymphatics, and as the secreting glands are primarily derived from these surfaces, it naturally comes about that they are in free communication with the lymphatics and lymph glands. It follows that the lymphatics involved in the cancerous material convey the cancer elements to the associated lymph glands, and these may become so surcharged as to burst their capsules. Lymph glands enlarged in this way sometimes form very large masses, and it is not uncommon to find a primary carcinoma with a diameter of two centimeters associated with a collection of lymph glands as big as a fist. Lymph-gland infection varies in rapidity and degree; great differences occur not only in regard to cancer of particular organs, but also in relation to the same organ in different individuals. Occasionally lymphatic channels are so stuffed with cancerous material that they may be dissected from the connective tissue and traced to the lymph gland. Occasionally the ducts from the lymph glands about the receptaculum chyli and the receptaculum itself are so stuffed with cancerous material that they appear as cords, and the thoracic duct is sometimes found in this condition.

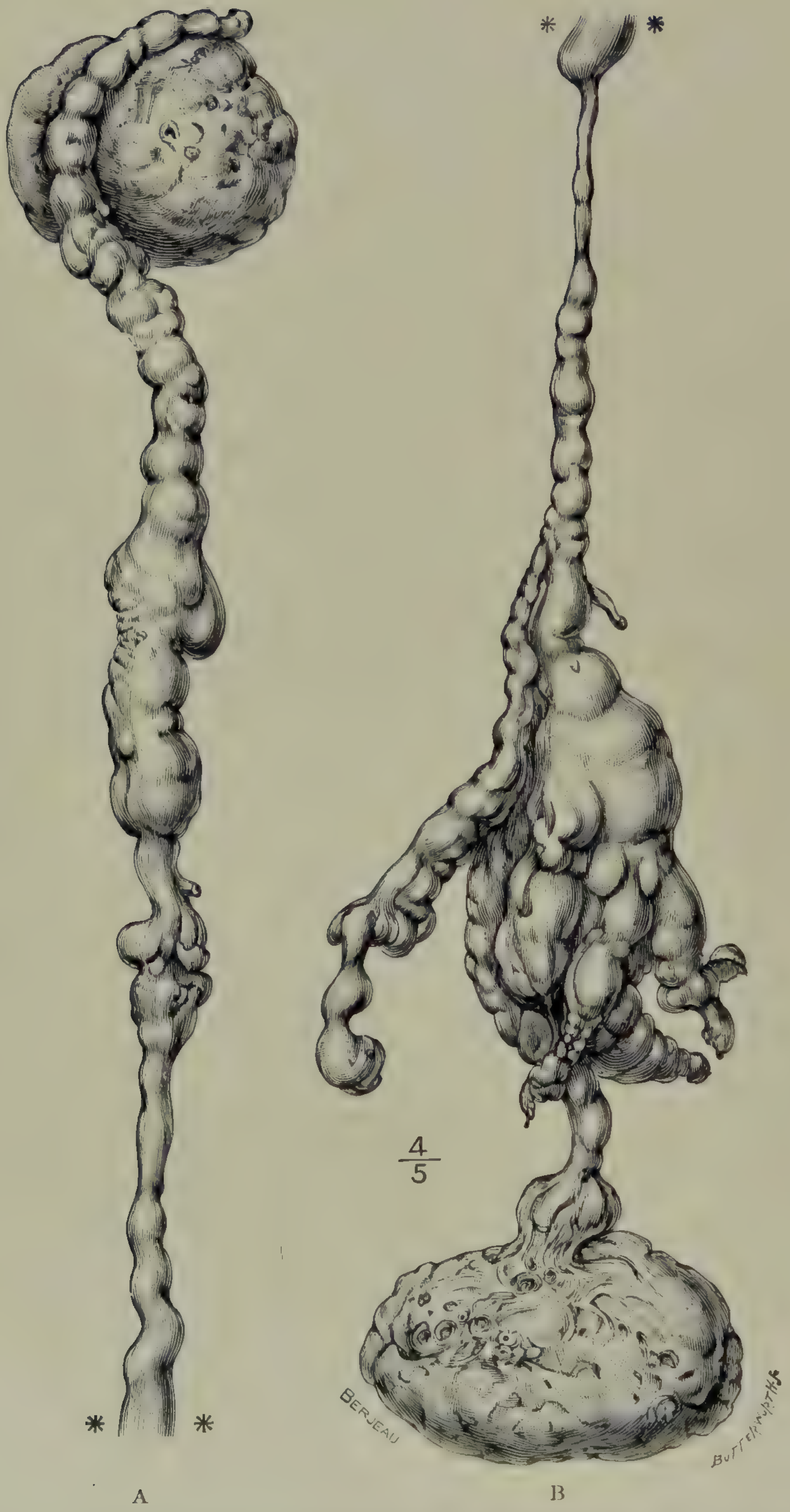

Fig. 213.—The Thoracic Duct and Receptaculum with some Adjacent Glands Stuffed with Cancerous Material Secondary to Cancer of the Rectum (Hillier).

A, The upper half, showing the termination of the duct on an enlarged cervical lymph gland; B, the lower half with the receptaculum and an enlarged lumbar lymph gland.

These observations are important because they offer an anatomic explanation of the existence of an enlarged lymph gland so often found at the root of the neck on the left side as a complication of cancer of the stomach. The existence of an enlarged gland in this situation is a diagnostic feature of great value, especially in a disease like cancer with so many delusive clinical features.

The relation of the growth to the wall of the duct shows that the implication of its structures is complete; it is not due to the mere blocking of its lumen with cancerous tissue resembling the clot in a thrombosed vein, but its walls are infiltrated with the cancerous tissue in the same way that sarcomatous tumors implicate the walls of large veins.

Obstruction of the thoracic duct by extension of cancer has been noticed in association with primary cancer of the stomach, uterus, and rectum, and careful descriptions of the condition have been published by Unger, Weigert, Troisier, and Hillier, among others.

Perhaps the most remarkable feature of the complication is the absence of any indication that the duct was obstructed, and in no case was chylous ascites observed.

The extent to which lymphatic infection has occurred is a matter which cannot be accurately defined in a given case of carcinoma, and this adds an additional factor of uncertainty in estimating the results and value of surgical procedure.

This lymph gland complication is always an element of danger. When the cervical glands are enlarged they interfere with the trachea and esophagus; they also become firmly adherent to the sheaths of big vessels, and as the glands break down the subsequent ulceration opens up the jugular vein or the carotid artery, and, in the inguinal region, the femoral vessels. Lymph glands when enlarged and stuffed with carcinomatous cells have a great tendency to soften in the center and form spurious cysts. When the skin becomes implicated large portions of the infected glands slough and leave large horrible holes, from which foul fetid fluid issues, while the edges of the chasm produced by the sloughing continue to extend and involve the neighboring tissues.

The size of the cancerous mass produced by the infected lymph glands and the tissue infected by them when they become so stuffed with cancer that they burst their capsules is often, as has already been mentioned, out of all proportion to the initial lesion; indeed, in many instances the patients are little troubled by the primary ulcer, which may be so small and inconspicuous as to escape observation until the enlargement of the lymph glands compels the patients to seek advice, which leads to a search for the primary lesion. It is not uncommon, when this focus is situated in a recess in the mouth or pharynx, for the cancerous ulcer to be so small as to be completely overlooked. Then the disease is described as a primary squamous-celled carcinoma arising in lymph glands, or, in the neck, it is sometimes attributed to epithelial vestiges of the branchial folds. It is also possible that the primary focus undergoes retrogressive changes and heals spontaneously, but the gland infection proceeds to the patient's destruction. I have seen this happen on the scrotum twice.

Dissemination.—Cancers are extremely prone to dissemination, and the secondary growths resulting from the deportation of minute fragments of cancer may appear in any organ or tissue. The cells that give rise to secondary nodules are transported by lymph and blood vessels and by an insidious process known as permeation. When these minute emboli and cancer particles lodge in suitable positions they multiply and thus give rise to a growth which in its histologic features exactly resembles the parent tumor. So faithful is this reproduction that the nature of the primary tumor can often be correctly inferred from a microscopic examination of a secondary nodule.

The amount of dissemination varies greatly. In some cases secondary deposits will be found only in the liver, while in another and apparently identical case, in so far as the structure of the tumor is concerned, secondary knots occur in almost every organ of the body, including the skeleton. In the case of squamous-cell cancer it cannot be said that secondary deposits are rare, but dissemination certainly happens far less frequently, and never so extensively as in cancer arising in secreting glands. It is also noteworthy that the squamous-cell variety is, in some situations, more liable to disseminate than in others. For example, secondary deposits are rarely met with when this disease attacks the larynx, and the mucous membrane in relation with the mandible or maxillæ, and the esophagus. The explanation sometimes offered of this peculiarity is that carcinoma in these situations usually runs a rapid course, and often destroys life so quickly that the period is too short to allow of the formation of secondary nodules. This is inadmissible, for in cancer of the scrotum dissemination is almost as exceptional as when the larynx is attacked.

Secondary deposits of cancers are not always so small as merely to merit the name of knots, but form occasionally tumors of some magnitude.

The vitality and power of independent growth possessed by minute detached portions of carcinoma is very remarkable. These minute epithelial emigrants not only live and grow, but they reproduce the peculiarity of the primary cancer. It is astonishing to find a secondary cancerous deposit in the humerus with all the characters of the glands of the rectum; a multitude of secondary nodules in the skin with the structural features of gastric glands; nodules in the lungs exactly reproducing that peculiar form of hepatic carcinoma which arises in the biliary ducts; the familiar closed follicles of the thyroid gland reproduced in the body or spinous process of a vertebra; nodules resembling the structure of mammary carcinoma in the ovary, brain, or choroid coat of the eye; and a mass growing from the frontal bone with all the characters of the prostate gland, secondary to cancer of that organ. It is one of the great triumphs of pathologic histology that it has demonstrated that carcinoma takes its type of epithelium from the secreting gland in which it arises.

This power of independent growth possessed by the epithelium of cancer is a very dangerous feature, and does not always need blood or lymph vessels for its manifestation. It sometimes happens that an abdominal viscus is attacked by cancer, and a small outgrowth makes its way through the peritoneal covering, bursts, and sheds its cells into the general peritoneal cavity; these are distributed by the peritoneal fluid and the movements of the bowels, and in a few weeks the whole of the serous membrane will be dotted with hundreds, and sometimes thousands of nodules, each reproducing the type of the parent tumor. This mode of epithelial infection of the peritoneum I have found in cancer of the gall-bladder, ovary, and especially in cancer of the body of the uterus; no form of dissemination gives rise to such innumerable secondary nodules as this, nor demonstrates in a more remarkable way the power of epithelium to engraft itself, to live, and to grow.

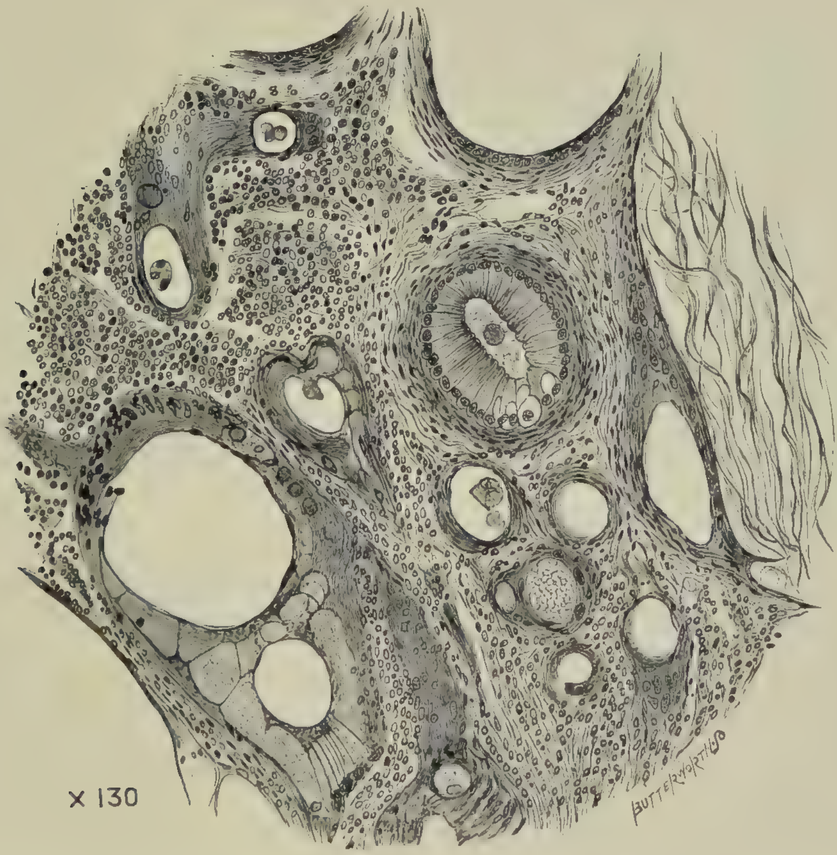

FIG. 214.—SECTION THROUGH A PORTION OF AN INGUINAL LYMPH GLAND INFECTED WITH CANCER (after Foulerton).
The primary disease was in the rectum.

Secondary deposits of cancer may occur in any organ and tissue of the body; my own observations teach me that among the malignant epithelial tumors, cancers of the breast and of the pylorus give rise to the widest form of dissemination; thus cancer is very infectious to the individual affected with cancer, but not to others. The rarest of all tissues in which to find secondary deposits is voluntary muscle, and the rarest of all organs is the heart. Secondary deposits are even met with in the eyeball, and it is a curious fact that the great majority of cases occur in association with mammary cancer, and in one exceptional case both eyeballs contained secondary nodules. Secondary infected deposits in the globe have also been observed in connection with cancer of the stomach and thyroid gland.

Secondary Cancer of the Lung.—The extraordinary frequency with which the lung is infected with malignant disease, whether sarcoma or carcinoma, is due to the circulation. In the case of sarcoma the particles gain the circulation entirely through the veins, and in the case of carcinoma the cancer-emboli may also enter the blood-stream by the veins; but the most usual channel is the right lymphatic duct or the thoracic duct, according to the situation of the primary focus of disease. In this event, of course, the migratory elements are discharged into the innominate veins, and as they are forced into the pulmonary vessels, they become filtered from the blood by the capillaries of the lungs, and after their arrest, find in the vascular tissue an excellent soil in which to grow.

In discussing secondary deposits in the lungs due to cancer-emboli, it must not be forgotten that cancer of adjacent organs, such as the mammary glands, the esophagus, stomach, etc., may locally invade the pleura (permeation) and give rise to a widely scattered crop of miliary nodules on the pulmonary pleura. This mode of infection must be distinguished from that in which the lungs are infected by emboli transported by the blood.

Much new light has been thrown on the way in which cancer implicates the chest wall and infects the thoracic as well as the abdominal organs by the researches of Handley, who has especially studied the manner by which cancer cells slowly creep along the planes of fascia.

Dissemination by Permeation.—Handley has made a very careful investigation of the mode by which cancer of the mamma spreads in the thoracic walls by a slowly progressive centrifugal serpiginous process, which is an actual growth of the cancer along one or other lines of the parietal layers in continuity with the primary growth. He has carefully analyzed the situation of secondary deposits in this disease and points out that they appear in the near neighborhood of the primary focus, and that as the disease advances the nodules appear at greater distances from the primary focus until at last, if death is unduly delayed, they appear in the trunk-ends of the limbs. Hence the distal halves of the limbs enjoy an almost invariable immunity from the cancerous nodules. This applies to the bones of the limbs as well as to the skin. He believes that these facts indicate that the superficial spread of cancer takes place by permeation of the deep fascia. Moreover, he has carefully studied and traced this infiltration of the deep fascia microscopically.

Handley thinks that visceral dissemination in mammary cancer does not commonly take place by way of lymph glands and the blood. He shows that it occurs through the fine anastomotic lymphatics which pierce the parietes and then infect the subserous lymphatics of the pleura and peritoneum. Cancer cells then escape into the thoracic and abdominal cavities, implant themselves on the surface of the viscera, and give rise to the deposits which terminate the life of the patient. (This will be referred to in describing metastatic cancer of the ovary.)

Transference of Cancer by Contact.—Many cases have been reported which are supposed to prove that cancer may be transplanted by the direct contact of a cancerous surface either with another part of the infected person's body or with another person. The example of the first condition usually mentioned is infection of the skin of the arm from contact with an ulcerating cancer of the breast; or the infection of a labium by a squamous celled cancer in the opposite labium. I have never seen the upper lip infected from contact with a cancerous lower lip. Surgeons who are actively engaged almost daily in performing operations for cancer frequently cut or prick their fingers, but a cancer transplanted in this way is unknown. This should make us careful in accepting evidence in regard to what is sometimes called *cancer-a-deux*, in which a man cohabiting with a woman suffering from cancer of the neck of the uterus has a cancerous ulcer appear on his penis and *vice versâ*.

Cancer Infection.—It has long been known that normal cutaneous epithelium, when accidentally engrafted into subcutaneous tissue, the cornea, or the iris, will live and grow. It has also been demonstrated beyond all cavil that when women have been ovariotomized, especially in cases of large ovarian adenomata, growths have in some instances arisen in the abdominal cicatrix; these on microscopic examination have displayed cysts furnished with the regular large mucin-bearing cells so characteristic of some varieties of ovarian tumors (adenomata). As these tumors in the cicatrix have been unassociated with any recurrence in the pelvis, or secondary nodules in the peritoneum or in the viscera, the conclusion is irresistible that they were due to infection of the edges of the abdominal incision in the course of the ovariotomy. These cases are profoundly interesting because they illustrate what often happens in the course of an operation for the removal of a cancer; and it is this local soiling of the wound with minute cancerous particles that constitutes the accident which I have called cancer-infection.

A careful study of the clinical aspects of cancer, as well as the most critical inquiry in the post-mortem room, has convinced many that cancer exhibits peculiarities in regard to mode of growth, infection of lymph glands, dissemination, and the way it destroys life, according to the gland in which it arises. Even this only partly expresses the real truth, for the course of carcinoma of the same gland is not only widely modified by age and constitution, but the same disease in two patients, apparently alike in age and environment, will progress so differently that no surgeon can predict with any reasonable certainty the expectancy of life, result of operation, liability to dissemination, or the chances of recurrence. Therefore, in deciding whether it will be to the patient's advantage to have a cancerous organ extirpated, the surgeon is guided by the known peculiarities of the particular organ affected, the extent to which the adjacent tissues are implicated, the degree to which the associated lymph glands are infected, and the absence of signs indicating dissemination. In spite of every care, the operation is occasionally followed by such rapid local recurrence that the course of the disease is accelerated rather than retarded.

It is a fact which every surgeon who has had much experience in operating for cancer must have noticed that, in some instances where he has conducted carefully planned but extensive operations for cancer, the patient has had rapid recurrence, and the disease has manifested itself in a manner far worse than when left to run its natural course. This phenomenon, I believe, may be explained. In removing the affected organ the infected lymphatics and blood-vessels stuffed with the cancerous material are divided, and the cancer cells are let loose over the damaged tissues, which they infect, and lead to an extensive outbreak of local cancer. Knowledge of this kind is important, because it leads us to exercise greater care in keeping well wide of the diseased area while removing it; and though we cut out the cancer with its implicated lymphatic ducts and infected lymph glands, we should exercise every precaution not to incise the diseased parts, and thus unwittingly scatter the diseased cells over the denuded surfaces.

I have more than once seen patients who had been submitted to operation for mammary cancer, and in whom the removal had been imperfectly carried out, present on both sides of the scar a series of cancer nodules at each stitch hole due to infection by the needle and thread in the course of the operation.

Heredity.—This is a vexed question in regard to cancer because so much that appears to be affirmative is founded on false facts or circumstances that cannot be tested or proved. The question of cancerous inheritance bristles with difficulties many of which are at present insuperable.

De Morgan Spots (**Canceroderms**).—It is not uncommon to find on the skin, especially of the abdomen and chest of patients debilitated by cancer, numbers of small raised red spots looking like nævi. These are often called "De Morgan spots," after Campbell de Morgan (1872), who regarded them as almost pathognomonic of cancer. They are patches of pigment and not nævi, and though frequent in cancerous patients, are very often present in the non-cancerous after middle life.

These spots have been carefully studied by Brand and Leser. Their conclusions are of interest, for they point out that the "spots" do not appear in healthy subjects, or in persons suffering from other diseases in early or middle life, and never, even in old age, in large numbers. When these spots are plentiful there is every reason to suspect cancer.

I cannot endorse this opinion; for twenty-five years I have devoted very careful attention to this matter in the Middlesex Hospital, and believe these spots to be a common accompaniment of the cutaneous changes met with after middle life.

The Cause of Cancer.—The pathogenesis or cause of tumors and cancer has always been a fascinating subject of inquiry, and has led to much speculation, some of which has had great influence in directing investigation into special lines. One of the most interesting of these speculations we owe to Cohnheim, and it may be called the embryonic hypothesis, for he imagined that tumors and cancers arose from unutilized fragments of tissues, or residues, some of which may be due to faults or embryonic irregularities. Such residues, "rests," or tumor-germs may early in life, even in the fetus, develop into tumors, or remain many months, or even years, quiescent, then suddenly, and apparently without provocation, take on active growth. This theory, unsupported as it was, without the least evidence of a concrete character, was advanced by Cohnheim as an explanation of the origin of connective-tissue and epithelial tumors. The great argument against it was to the effect that unutilized embryonic tissue (tumor-germs) had not been demonstrated. The theory, however, indicated a line of inquiry in which observation and experiment have demonstrated, in regard to some genera of connective-tissue tumors and very many dermoids, that it offers a solution of several difficult problems.

It is desirable to arrange tumor-germs in two groups—vestiges and rests. The term *vestige* should be reserved for remnants of organs functional in vertebrates lower than man; for those organs that are of importance to the embryo, but useless in the adult; and a few which, though utilized in the male, are useless, or almost useless, in the female, and *vice versâ;* as well as for those structures which, as far as we know, serve no useful purpose in any vertebrate at present living, but were doubtless of importance in their ancestors, *e. g.*, the mesonephros, the parovarium, Gärtner's duct, the urachus, the vitello-intestinal duct, the central canal of the cord, etc.

The term *rests* should be reserved for detached fragments of glands and isolated portions of tissue and epithelium.

The easiest demonstrable example occurs in connection with the *spleen.* It is the normal condition to find in the gastrosplenic omentum of a child at birth a miniature spleen or splenculus. It is no uncommon event to find two or three splenculi, and as many as five have been counted. In many instances these accessory spleens atrophy, but frequently they may be detected in adults. When the abdominal viscera are transposed the spleen is, as a rule, represented by a cluster of splenculi.

The *pancreas* furnishes a similar example. Several instances have been recorded in which an accessory pancreas has been detected. It is usually situated in the wall of the duodenum or jejunum, between the serous and muscular coats, and it is important to remember that these detached fragments may occur at some distance from the main gland, and they are not uncommon in the wall of the stomach. *Accessory thyroid glands*—neglecting those which lie in the tract of the thyroglossal duct—have been detected on a level with the episternal notch, and on the trachea as low as its bifurcation.

Rests associated with an *adrenal* occur in the kidney, immediately beneath the capsule, as yellowish-white nodules; they have been described as renal lipomata, and there is reason to believe that they are occasionally the germs of very large tumors. Adrenal rests have been found under the capsule of the liver; along the course of the spermatic artery, and in the spermatic cord; also on the peritoneum near the ovary.

Detached fragments of *liver* occasionally occur in the falciform ligament and in the neighborhood of the transverse fissure; but no one, so far as I know, has succeeded in demonstrating the origin of a tumor from these rests; but it is easily conceivable that they might under exceptional conditions play the part of tumor-germs.

As fragmentary livers, so to speak, occur beyond the actual hepatic territory, it is much more probable that portions of glandular tissue may be isolated within the liver itself, and there are strong grounds for the belief that certain adenomata of the liver do arise from such sequestrated tracts of hepatic tissue. This mode of origin of adenomata gains strongest support from our knowledge of mammary tumors. Outlying pieces of *mammary gland* are occasionally met with, merely joined to the main gland by connective tissue, and it is reasonable to believe that they are the source of some of the encapsuled adenomata that occur at the periphery of the breast. The mammary rests must not be confounded with *accessory mammæ* arising as *neomorphs* in the adjacent skin, especially in the skin of the axilla. It is also probable that isolated encapsuled portions of gland are the source of the fibro-adenomata so common in the mammæ of young women. The same explanation holds good for some of the small cystic tumors of the *parotid gland.*

Tracts of epithelium occur as vestiges and as rests. As vestiges epithelial tracts occur in the tongue—the lingual duct; in the neck—branchial clefts; in the naso-palatine suture—Stenson's canal; in the brain—infundibulum; and in other situations the vestigial character of some of the tracts and their tendency to form tumors has been already described. The tumor-forming proclivities of others will be abundantly demonstrated in the section on Dermoids.

As "rests," epithelial tracts occur in the line of the meso-palatine suture, in the gums derived from enamel-organs, and in the lines of coalescence of the trunk, the scalp, and face. In these situations they give rise to tumors. Epithelial rests may be produced accidentally by surface epithelium carried into the deeper tissues by cuts, punctures, etc. These give rise to small tumors, when the conditions are favorable, known as implantation cysts (see p. 825).

Rests are known in connection with non-epithelial tissues, but they do not admit of such ready demonstration. In the neighborhood of epiphysial lines, particularly in the long bones of rickety individuals, islets of cartilage have long been known, and it is not unreasonable to believe that such belated fragments may be the source of some enchondromata and osteomata.

It is curious that many vestiges and rests lie latent several years. Take, for example, accessory thyroids; rarely they give trouble before puberty; many never cause the least inconvenience and a few become active even late in life. Goiter of the parenchymatous kind is occasionally congenital; but I am not aware that the cystic variety is common until the accession of puberty; after this event it is frequent. Mammary adenomata are of common occurrence between the sixteenth and thirtieth years, but they are almost unknown before the fourteenth year. The best instance of this sudden awakening may be studied in the parovarium; its ducts are quiescent during the early years of life. So far as I have collected the evidence—and my search has been a broad one—

there is no case on record of a parovarian cyst occurring in a girl under fifteen years. Between the ages of sixteen and twenty-five years a large number of parovarian cysts have been removed.

Papillomatous cysts of the ovaries are almost unknown before the twenty-fifth year of life. Certain it is that small cysts have been detected in infant ovaries, but these were not appreciable to clinical observation. The existence of tumor-germs is demonstrable in the case of cysts. There is scarcely a cyst known to which pathologists cannot ascribe an origin in some preëxisting duct, tube, gland, or vestige. One of the most extraordinary features connected with some cysts is the physiology of secretion. For instance, a parovarian or a simple ovarian cyst containing only two or three ounces of fluid in a tense sac with thin walls may, in spite of the intracystic pressure, continue to increase until it attains a capacity of three, four, or more gallons. Hydrocephalus and meningoceles illustrate the same inexplicable phenomenon, for they are devoid of glands and lack epithelium, at least in their late stages.

In the case of simple tumors we know that they arise from a matrix similar in structure to the tumor. These facts should cause us to keep a keener look-out for isolated fragments (rests) of organs and tissues. A very suggestive instance is a fatty tumor of the broad ligament of the uterus. Under normal conditions there is no fat between the layers of this serous ligament, yet lipomata have been observed in that situation, sometimes of great size. A careful examination of the parts has taught me that the parovarium is sometimes buried in a layer of rich yellow fat

The tumors to which Cohnheim's theory cannot be regarded as in any sense applicable are the sarcomata and carcinomata.

Although Cohnheim's theory of tumors concerns a limited number of genera, it commands attention because it is in itself a brilliant generalization, and has served a valuable purpose in directing inquiry upon particular lines, which has led to a great extension of knowledge in regard to vestiges and rests.

The embryonic theory is now discarded as an explanation of the origin of cancer.

The Parasitic Theory.—Many who are closely acquainted with the clinical and pathologic features of carcinoma feel strongly that this disease will be defined as *a chronic infective disease due to a micro-parasite which selects an epithelial cell.*

The brilliant results of microscopic inquiry of the last thirty years into the cause of disease have very widely extended our knowledge in regard to the number and variety of parasitic diseases, as well as indicating a selective power in choosing the organ and even the tissue most favorable to their development. For example, a *demodex* selects hair-follicles; *ankylostomum* prefers the mucous membrane of the small intestine; the malaria-parasite finds its way into an erythrocyte, while filariæ prefer the liquor sanguinis. The six-hooked embryo of *tænia echinococcus* has a preference for loose areolar tissue and *coccidium oviforme* finds its way into the epithelium of the biliary passages of rabbits.

Among infectious diseases the most extraordinary and some of the deadliest are those in which the infecting agent gains access to the body by inoculation, that is, through abrasions, cuts, or punctures of the skin or mucous membrane. Familiar examples of this are tetanus, hydrophobia, leprosy, glanders, actinomycosis, and syphilis. The point of inoculation is known as the primary focus of the disease, and at this source the parasites multiply, enter the circulation and lymph stream, whence they may be distributed throughout the body, often to form secondary foci of disease which interfere with the functions of the organs in which they may chance to grow, as well as interfere with the nutrition of the body by means of the toxins they brew and discharge into the blood, producing a form of slow poisoning.

The facts which support the parasitic theory of cancer may be summarized in the following way. In its initial stage the disease is purely local, then gradually spreads to the adjacent tissues and at the same time infects the lymph glands which receive the lymphatics from the affected area, and general infection of the body (dissemination) follows. Then there is the toxic effect (cachexia) upon the individual, often out of all relation to the extent of the disease. In many instances the disease seems to have a period of quiescence and then to enter on a period of recrudescence, exactly like a chronic infectious disease such as syphilis. The primary focus in this disease disappears after a time and leaves but little trace of its existence, so occasionally in carcinoma the primary focus may atrophy and become inconspicuous. The infectiveness and vitality of the cancer-cell has been already discussed and is a strong argument for those who are seeking for a parasite, but to my mind the most valuable evidence is supplied by the distribution of the initial lesions of cancer.

It is clearly established by a careful study of death-returns, that in more than half the cases in which death is attributed to cancer the primary seat of the disease is in the digestive organs. The distribution of cancer in that part of the alimentary canal which occupies the belly is somewhat remarkable. For example, the stomach is not only the commonest primary seat of cancer when compared with other digestive organs, but it stands third in order of frequency among all organs, the breast (mamma) being first and the uterus second in order of liability. The small intestine (duodenum, jejunum, and ileum) is very rarely attacked by cancer, but in the rest of the canal (colon and rectum) it is a very frequent disease. Even in its attacks on the big bowel cancer exhibits a partiality at present inexplicable, for it is common to find it in the rectum and sigmoid flexure, but its appearance in the vermiform appendix and ileocecal valve is phenomenal; and its presence in the cecum may be fairly described as unusual. It is as difficult to explain the comparative immunity of the ileocecal valve from cancer as to find an adequate cause for its excessive frequency at the pylorus.

Although the utmost vagary is exhibited by cancer in its topographic distribution in the alimentary canal, it is absolutely unfavorable to the embryonic theory, for the sites of the greatest events in its embryology are those which manifest the least liability to cancer.

The greatest feature which distinguishes carcinoma from all infective diseases is its property of producing secondary deposits which reproduce the structural details of the organ or tissue primarily affected, and this is one of the most surprising facts in the whole range of pathology. Reference will be made again to this remarkable vitality of epithelium in dealing with malignant embryomata. In the case of the typical infective diseases like tuberculosis the infective agents, the tubercle bacilli, are transported by the blood-stream, and we are prepared to find a colony of the bacilli flourishing in the cancellous tissue of the calcaneum or the body of a vertebra, and these will cause a tissue lesion identical with those which would be formed if the primary tuberculous lesion was situated in muscle, brain, lymph gland, lungs, or kidney. This means that the bacilli are transported but there is no actual transference of tissue.

The conclusion arrived at by the histologic study of carcinoma has induced the majority of investigators to realize that the disease essentially originates in epithelial cells, and these elements of cancerous formations have been most perseveringly studied with the assistance of excellent microscopes and anilin stains. The method of cultivating the cells in nutrient media has been prosecuted with great ingenuity, but so far has been barren in results. From time to time expectation has been raised that the microörganism has been found, but only to end in disappointment. The strict satisfaction of Koch's postulates must be fulfilled to satisfy scientific skepticism:

1. The microörganism must be present in all cases of the disease.
2. It must be capable of being cultivated apart from the animal.
3. It must reproduce the disease when inoculated into a healthy animal.

Up to the present no microörganism has been found which will satisfy even one of these postulates.

The Cytologic Transformations Observed in Malignant Tumors.—Among the most important observations which have been recorded in relation to the cells of malignant tumors (sarcoma and carcinoma) must be included those made by Farmer, Moore and Walker in relation to the nuclear division.

It has been known for many years that in the production of sexual cells (gametogenic tissue) in plants and animals the forms of nuclear division differ materially and in a highly complex manner from those found during the production of cells composing the tissue of the body, and the above-mentioned investigators have been able to trace in detail a number of definite and serial changes in the cells of invading and proliferating malignant tissue which are remarkably similar to those obtained during the maturation of the elements contained within the sexual reproductive glands, and this resemblance extends even to minute points of detail.

These observations show that the various types of malignant growths present certain features in their cytologic transformations common to all, and that these features are similar to those to be observed in the process of differentiation of reproductive cells from the preceding somatic tissue. The evidence, the investigators believe, justifies them in correlating the appearance of these "gametoid" neoplasms with the result of a stimulus which has changed the normal somatic course of cell development into that characteristic of reproductive (not embryonic) tissue. These peculiar nuclear changes have not been observed in innocent tumors.

The same biologic triad of investigators has succeeded in showing that the remarkable vesicular structures found in cancer cells known as "bird's-eye inclusions" or Plimmer's bodies occur normally in cells during the production of sexual elements in vertebrata. These bird's-eye inclusions consist of a well-defined wall enclosing a clear fluid in which is suspended one or more darkly staining granules. In size they may be very minute or equal the nucleus. One, or as many as twenty occur in the same cell; they commonly lie adjacent to the nucleus, which they frequently press, giving it a crescentic appearance. These bodies are very conspicuous and were long regarded as peculiar to malignant growths; they acquired some notoriety on account of their resemblance to *Plasmodiophora brassicæ*, discovered by Woronin in 1876 as the cause of a disease of the edible *cruciferæ*, especially cabbages; this relationship, however, has not passed beyond the bounds of speculation.

Now that Farmer and his co-workers have shown that the *archoplasmic vesicles*, as they have been called, appear during spermatogenesis in vertebrates, and are, to all appearance, structurally identical with, and arise in a manner similar to, the "bird's-eye inclusions" in the cells of cancer (Plimmer's bodies), it rather weakens belief in their specificity for malignant growths.

The peculiar nuclear changes observed in the cells of malignant growths do not affect all the cell-elements equally; those which show the changes in the highest degree are "situated in a zone behind the growing edge of the advancing neoplasm."

In the slow-growing tumors which produce a considerable amount of normal somatic tissue (fibrous tissue) cells showing the phases here referred to are far more difficult than in the rapidly growing tumors. In such growths, cells showing the figures of ordinary somatic division are numerous in comparison with those showing heterotype figures. This would seem to indicate that the cells which are destined to form fibrous tissue never divide heterotypically.

These observers look upon this remarkable transformation as representing the immediate cause of development of the malignant growth, but the remote cause, the specific irritant, has yet to be found. Nevertheless these interesting changes which they have detected constitute a valuable and interesting item in our knowledge of the cytology of malignant tumors.

In order to emphasize the difficulty of what may be, for convenience, termed the cancer-question, it is necessary to mention that competent pathologic and bacteriologic investigators who have undertaken the most painstaking and laborious researches with the hope of discovering the cause of carcinoma and sarcoma are divided into two camps, namely, those who strongly believe that it is due to a micro-parasite, either a bacterium or some lowly animal form such as a protozoan; and those who think the disease is due to some altered conditions of the cells independent of parasites. The position for the non-expert in this matter is illustrated by the following lines from the speech of "Empedocles on Etna":

The Gods laugh in their sleeve
To watch man doubt and fear,
Who knows not what to believe
Since he sees nothing clear,
And dares stamp nothing false, where he finds nothing sure.

Treatment.—The only method which offers any hopeful prospect to individuals affected with carcinoma *is early and thorough removal of the affected part with the associated lymphatics and lymph glands.* This mode of treatment can be adopted when patients seek advice at an early and operable stage. There are few organs in the body which have not been extirpated for this cause, *e. g.*, the mamma or breast, the eyeball, tongue, larynx, parts of the esophagus, stomach, long segments of the large intestine, including the cecum and rectum; the kidney, prostate, and sections of the bladder; the penis, testicle, ovary, and uterus; the gall-bladder and segments of the liver. There is nothing in the way of surgical ingenuity and enterprise that has been left undone with the hope of giving relief to sufferers from this disease, yet it baffles surgical art by its insidious growth, its indefinite limitations in the tissues, its infection of the lymphatic system, and its property of quiescence for many years and then of recrudescence.

Inoperable Cancer.—When carcinoma recurs locally after operations, or in its incidence involves vital parts which cannot be subject to operative interference, or affects an area of the body too wide to admit removal, much can be done to make the patient's condition more or less tolerable, and many methods of treatment have been devised with the hope of checking its growth.

Among the most remarkable of these is the performance of bilateral oöphorectomy for the purpose of inducing regression of inoperable and recurrent cancer of the breast (mammary gland). Dr. Beatson, after careful reasoning on the effect which double oöphorectomy is supposed to exercise on the mammary glands, advocated the removal of the ovaries and Fallopian tubes, and the administration of the extract of thyroid gland; the object being to promote and hasten the fatty degeneration of the cancer elements.

The results in some instances where bilateral oöphorectomy has been performed have been astonishing. In some patients the disease has completely disappeared; in others the disappearance has been followed by recrudescence. In many women the operation has temporarily checked the course of the disease, but in the majority it has had absolutely no effect. Bilateral oöphorectomy is not likely to take a permanent place in the treatment of inoperable cancer.

Great interest was aroused by the statement that the application of the x-rays has a remarkably deterrent effect on the growth of cancer.

The matter has been tested in the most determined way by very competent men, and it may be stated that the effects of this mode of treatment are local and only affect deposits of malignant disease which are exposed; it is impossible without injury to the skin to administer a sufficiently strong exposure to modify growth in the viscera, although a moderate exposure relieves deep-seated pain. When superficial growths are exposed to the rays, pain is usually relieved, growth is retarded, and retrogressive changes induced which sometimes enable patients to resume an active life.

The judicious exposure of rodent ulcer to x-rays or to radium not only heals the ulcers but cures the disease, and, what is remarkable, leaves a scar which resembles the normal skin more nearly than any scar resulting from a surgical operation. No drugs are known which in any way retard the growth of cancer. Periodically, remedies are vaunted, and claimed as specifics in this disease and are tried extensively by those affected with carcinoma. The drugs which have in recent years claimed attention more than others are Chian turpentine and salicylate of soda; in very exceptional cases some amount of improvement has been noticed in the rate of growth of large exuberant cancerous masses, and these drugs seem also to check the amount of discharge, but no real and permanent good has ever been recorded.

The list of things recommended as remedies by lay persons to their friends who suffer from cancer is almost inexhaustible, and includes powdered oyster-shells, violet leaves, and things unmentionable, as well as such incongruities as the witches add to the stew in the famous cauldron in the opening scene of "Macbeth."

The Toxin and Serumtherapy Methods.—It has often been observed by surgeons that when erysipelas attacked a cancerous breast the growth of the cancer appeared to be checked for a time; it was also noticed that after a breast had been removed for cancer and the wound became infected with erysipelas recurrence would be delayed longer than in ordinary circumstances. The discovery that erysipelas is due to infection by a streptococcus led to the idea of injecting inoperable malignant tumors with the toxins of the streptococcus of erysipelas and the Bacillus prodigiosus.

This method was introduced by Dr. Coley of New York. The mixed toxins act upon sarcomata so as to produce a rapid necrosis and fatty degeneration. Coley's original observations were published in 1891, and he has since given his later results (1906) with a table of 36 cases treated by himself and a table of 60 in which the methods have been carried out by other surgeons. The results have in some instances been brilliant. Some examples of spindle-celled sarcomata disappear by slow absorption, but the highly vascular round-celled forms are more likely to degenerate rapidly with the formation of sloughs. The more vascular the tumor, the more likely is the injection of the toxin to be followed by severe reaction which may be fatal. The best results follow in spindle-celled sarcomata. The method has had no permanent result in melanomata. The use of the toxin is not free from risk; its use is encouraging, but by no means certain.

In regard to the various methods advocated for the relief and "cure" of inoperable cancer it may be stated that all the methods hitherto proposed are unreliable and uncertain. In the majority of cases they have no effect whatever, and even in the few instances in which the treatment has done good there has been no reliability as to the permanency of the improvement.

It is clear to the minds of all thoughtful men that no permanent advance can be made in the treatment of this dire disease until we know the cause of it, and then it is highly probable that we may learn how to prevent it. The cause of cancer and sarcoma remains a riddle, but one which will be read, and, let us hope, speedily.

Palliative Treatment of Inoperable Cancer.—Apart from any hope of cure, much may be done to make men's and women's lives endurable in the late stages of inoperable cancer. To keep the fungating masses clean by frequent dressing, to check the discharge by absorbent powders, and to amend the horrible fetor by the use of antiseptic solutions, mercuricide powder, and ointments containing eucalyptus. The careful use of purgatives and variations in diet are often of very great importance. The administration of alcohol in any form in a lavish and free-handed manner is a grave mistake and as reprehensible as the unrestrained use of morphin.

Alcohol taken in the same moderation with food as the patient has been accustomed to in his usual manner of life is useful and harmless, and the administration of one-third of a grain of morphin twice daily is all that is necessary even in cases of great and severe pain; it is sufficient to give these patients comfort and keep them in that state of mind in which they can appreciate the visits of their friends and take an intelligent interest in things around until death relieves them.

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GROUP IV.—TUMORS ARISING FROM CHORIONIC VILLI—CHORION-EPITHELIOMA (DECIDUOMA).

In 1889 Sänger and Pfeiffer independently described a variety of malignant disease arising in the uterus presenting microscopic characters so strongly resembling decidual tissue that the disease was named *decid-*

uoma malignum. Subsequent investigations by other observers brought to light the important fact that this remarkable disease is very liable to arise in the endometrium within a few weeks or months of abortion, or delivery at term, and especially after the expulsion of the so-called "hydatid mole." Moreover, the microscopic investigation of the tumor showed that it conformed in histologic type to the multinuclear mantle or syncytium which covers the chorionic villus. This discovery led to a change of opinion as to the source of the disease, and as most writers regard it as arising from changes in the epithelial elements of the chorionic villi rather than in the decidua, the name chorion-epithelioma has come to be adopted in preference to deciduoma.

Before considering the essential features of this disease the change in the chorion known as the hydatid mole needs a brief description.

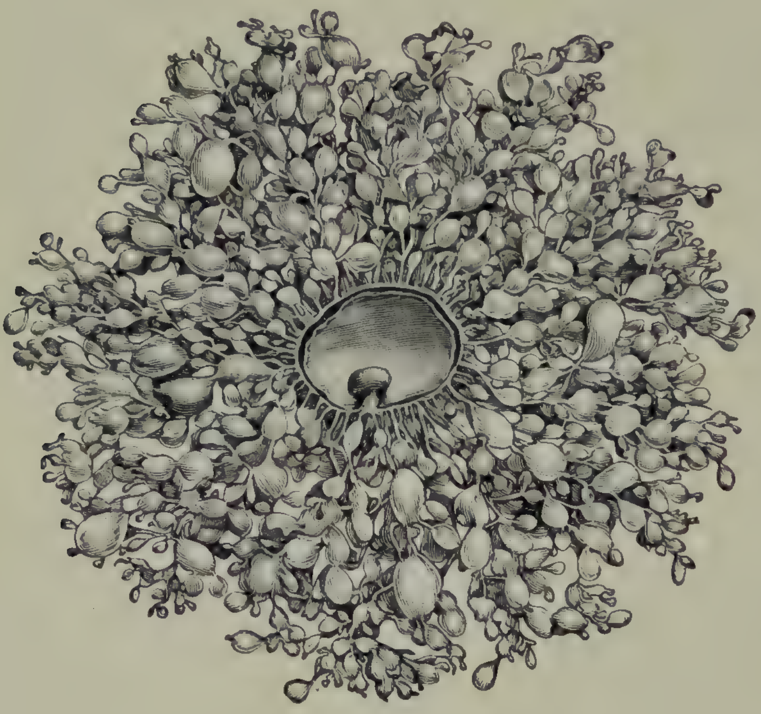

FIG. 215.—HYDATID MOLE (after Bumm).

The normal villi of the chorion in the early stages of their development consist of an axis or core of delicate connective tissue covered with epithelium arranged in two layers: the inner is known as *Langhans's layer;* the outer, called the *syncytium,* is peculiar, and resembles a large elongated multinucleated cell enveloping the villus like a mantle. In the early stages the connective-tissue core of the villus is devoid of blood-vessels; the tissue in the early stages consists of branching cells separated from each other by mucoid intercellular substance. Later, the cells become spindle-shaped and the tissue denser and vascularized.

In the disease known as "hydatid mole" the villi become changed into transparent grape-like bodies and look not unlike the vesicles so characteristic of the cystic stage of *Tænia echinococcus* (hydatids), and a hundred years ago the grape-like or vesicular bodies were regarded as hydatids, especially as the embryo is rarely to be found in these specimens.

In 1827 Madame Boivin and Velpeau showed that the disease depended on a change in the chorionic villi. Virchow gave attention to the histology of these vesicle-like bodies and considered them to be due to a myxomatous change in the villi (1853). This view prevailed until Marchand in 1895 demonstrated that the essential feature of the change depended more on the epithelium than the stroma of the villus, for it underwent irregular proliferation and assumed invasive characters, penetrating the decidua and even the muscular wall of the uterus. The vessels of the villi disappeared, the stroma degenerated, and the swollen condition of the so-called vesicles was the result of edema rather than mucoid change. The invasiveness or destructiveness of these altered villi has long been recognized, and specimens have been observed in which the villi have perforated the uterus and caused fatal bleeding into the abdominal cavity.

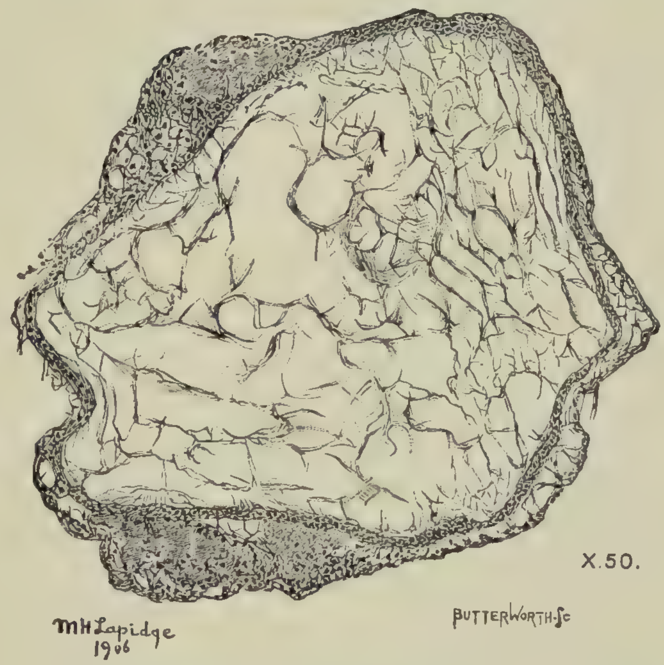

FIG. 216.—MICROSCOPIC APPEARANCE OF A CHORIONIC VILLUS FROM A HYDATID MOLE, IN TRANSVERSE SECTION, UNDER A LOW POWER.

The **hydatid mole** (or *chorion-epithelioma benignum*) is not common; its relative frequency has been estimated by one writer (Madame Boivin, 1827) to occur once in 20,000 pregnancies, and by another (Williamson, 1899) once in 2,400. It is quite certain that only a small proportion of women who have expelled hydatid moles suffer from malignant chorion-epithelioma, but no reliable estimates are available. The liability of a woman who has had a miscarriage of this kind to be the victim of such a deadly disease as chorion-epithelioma malignum renders it advisable

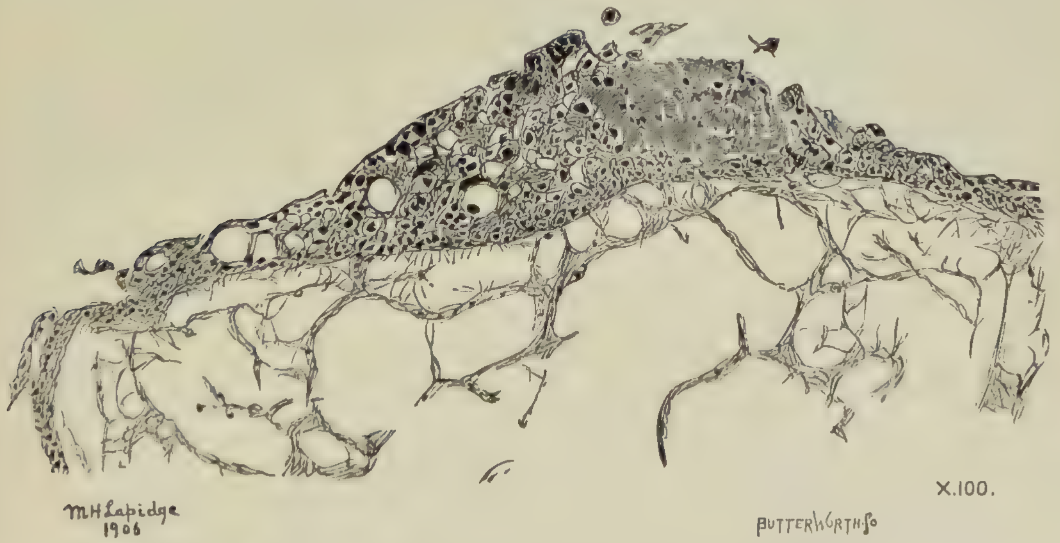

FIG. 217.—A PORTION OF THE CHORIONIC VILLUS SHOWN IN FIG. 216. More highly magnified with a portion of decidua attached to it.

that she should keep under medical supervision for some months after such an event.

Some writers are disposed to believe that there are two varieties of the hydatidiform mole: one being purely innocent and the other giving rise to the malignant chorion-epithelioma. As yet microscopic inquiries have not provided these theoretic distinctions with a histologic foundation.

The Relation of the Hydatid Mole (Chorion-epithelioma benignum) to Lutein Cysts.—Some valuable observations have been made on the frequent association of bilateral lutein cysts of the ovary and the so-called hydatid mole; indeed, the presence of lutein cysts in this disease is constant enough to lead to the belief that the two conditions are correlated. The lutein cysts are large enough to be of clinical importance, and they have been known to obstruct delivery, and in one instance to cause acute symptoms by undergoing axial rotation.

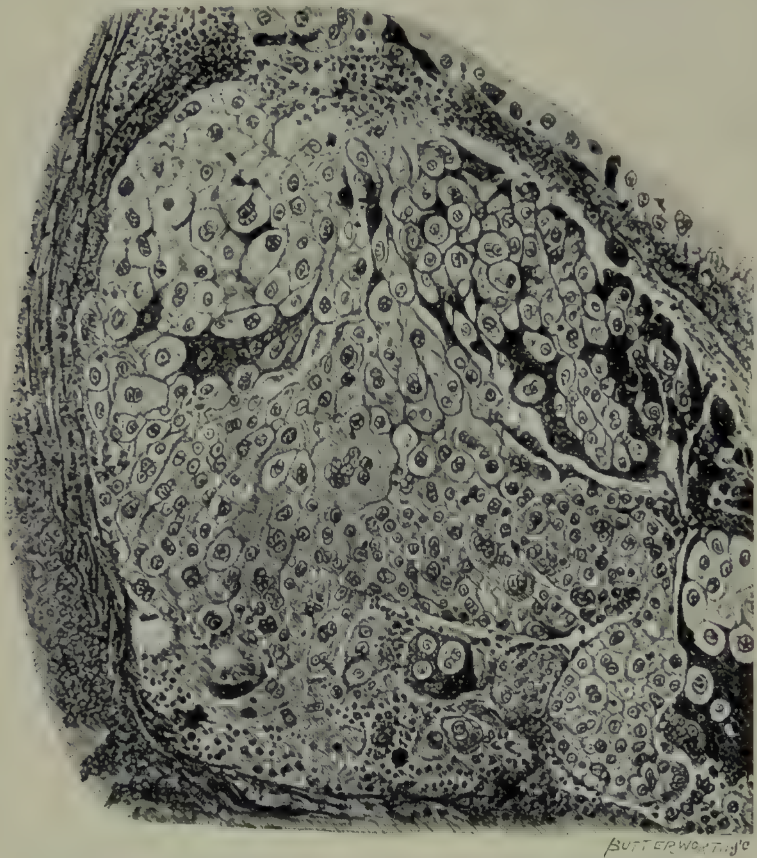

FIG. 218.—MICROSCOPIC CHARACTERS OF A CELL MASS FROM A CHORION-EPITHELIOMA. × 330 (after John H. Teacher).
Showing large decidua-like elements, and the forms intermediate between the Langhans layer and the syncytium.

This has given a new interest to the yellow tissue which composes the greater part of a corpus luteum, and some observers state that it furnishes an internal secretion, and that the adhesion of the oösperm to the endometrium depends on a proper supply of lutein secretion.

Fraenkel has elaborated this theory, and his views receive the support of some competent German pathologists; an overproduction of this secretion, the result of a plus quantity of lutein tissue, sets up, according to Pick, a "chorio-epitheliomatous reaction" in the embedded ovum and leads to the formation of a benign chorion-epithelioma (hydatid mole).

Lockyer has made a careful study of this question, and the result of his inquiry lends support to the view that there is a close correlation between lutein cysts and chorion-epithelioma of both kinds.

Chorion-epithelioma Malignum (Deciduoma).—The uterus when attacked by this disease usually enlarges and often becomes big enough to be appreciable as a tumor in the hypogastrium; its contour may be nodular. In some patients the disease is limited to the endometrium and the primary focus of the disease may be so small as not to cause enlargement of the uterus Some very exceptional cases have been described in which the disease did not involve the uterus but began in the vagina.

The intimate dependence of chorion-epithelioma on changes associated with pregnancy is illustrated by the fact that this disease occurs primarily in the Fallopian tube as a sequel of tubal pregnancy (see Riesel).

The result of the examination of a large number of examples of this disease by many investigators has established the fact that it arises in portions of the chorionic villi which remain embedded in the endometrium after the expulsion of the main products of gestation, and especially if the villi have undergone hydatidiform change. This relationship is particularly well shown in Fig. 219.

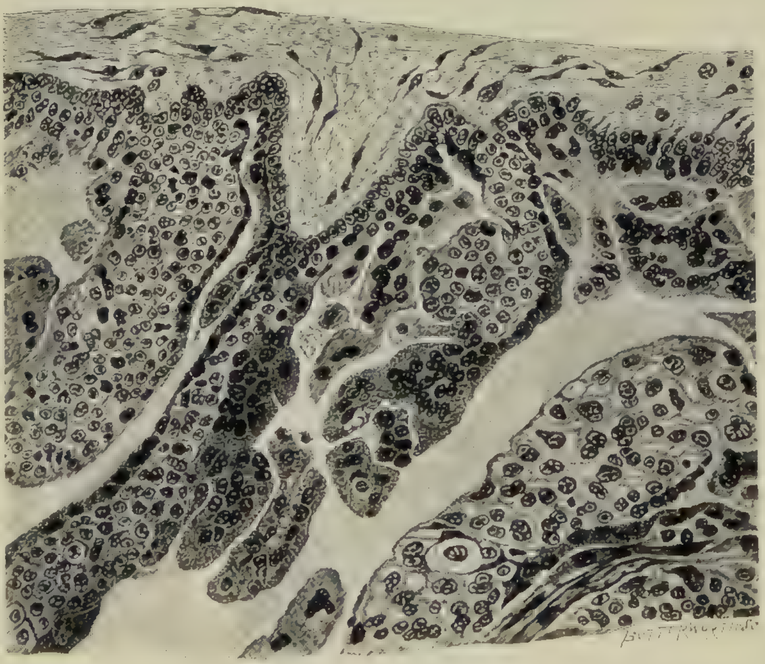

FIG. 219.—PORTION OF A CHORIONIC VILLUS FROM A CHORION-EPITHELIOMA (after John H. Teacher).

Showing the origin of the tumor from the epithelium it shows the continuity of the various cell-formations with one other layer of the villus.

Some competent authorities still believe that there may be two varieties of this disease, one arising from the epithelial elements of the chorionic villi and the other in decidual tissue.

To the naked eye the tumor tissue appears on section as a soft reddish mass. "Histologically a chorion-epithelioma consists of well-defined cells of various shapes and sizes closely packed together, and large multinuclear irregular masses of protoplasm in which no definite cell masses are recognizable. This tissue invades and destroys the uterine tissues after the manner of a malignant growth. It contains no proper connective-tissue stroma, or blood-vessels of its own" (Teacher).

A remarkable feature connected with chorion-epithelioma is the discovery that certain intrathoracic teratomata and teratoid tumors of the testis contain tissue indistinguishable from that of chorion-epithelioma.

The eroding power of the cells of a chorion-epithelioma enables them to penetrate the tissues and gain entrance to veins; fragments are deported by the blood-stream to lodge in lungs, bones, and other viscera and grow into secondary deposits. The common situations for these deposits are the lungs and vaginal veins.

The course of the disease is marked by oft-recurring profuse bleeding from the uterus; rigors; pyrexia; great emaciation and the signs of dissemination, such as secondary nodules in the lungs, bones, and the abdominal viscera. The disease is fatal and runs usually a very rapid course.

The chief clinical signs are frequent bleeding from the uterus, producing great anemia, accompanied usually by enlargement of the uterus following a recent labor or miscarriage. Many of these signs are caused also by the retention of a fragment of placenta, or a uterine mole. In such circumstances the cervical canal should be dilated and the cavity of the uterus explored; any retained fragments of conception that are removed should be submitted to careful microscopic examination in order to establish a reliable diagnosis.

Treatment.—The most satisfactory method of dealing with this disease is prompt removal of the uterus. Teacher considers it reasonable to conclude that operation offers a fair chance of recovery, and that it may be done with some prospect of success in the face of the gravest signs of disease and even of metastasis having occurred.

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GROUP V.—TERATOMATA AND DERMOIDS (EMBRYOMATA).

Under these terms we have to consider three remarkable groups of tumors which in their type forms are as easily distinguished from each other as a butterfly and a buttercup, yet examples occur with such composite characters that it is difficult to assign them to a group. This is true in a measure of nearly all species of tumor and is due to our ignorance of their pathogenesis. The difficulty in regard to such compound tumors as dermoids and teratomata occurs particularly in relation with the male and female genital glands. The subject will be considered in the following order:

1. Teratomata.
2. Dermoids.
3. Dermoids (Embryomata) of the Female Genital Gland. (Ovary.)
4. Intrathoracic and Intra-abdominal Teratomata.
5. Dermoids and Hilum Tumors of the Male Genital Gland. (Testis.)
6. Malignant Tumors of the Kidney in Infancy.

Teratoma.—There are two forms of teratomata, external and internal. This section will be concerned with the external varieties. Internal teratomata are discussed on p. 843.

A teratoma is an irregular conglomerate mass containing the tissues and fragments of viscera belonging to a suppressed fetus attached to an otherwise normal individual.

It is a significant fact that external teratomata are found almost exclusively in connection with the vertebral column and skull.

Strictly, the consideration of teratomata belongs to that department of pathology known as teratology; but as certain species are so apt to be confounded with dermoids, it is necessary to give an account of them here.

In order to appreciate the nature of these singular malformations it will be necessary to consider the subject of conjoined twins, supernumerary limbs, and acardiac fetuses. In the animal and vegetable kingdom it occasionally happens that a single ovum gives origin to two embryos, which may be quite separate from each other (twins), or they may be united, a condition known as *conjoined twins*. Twins the product of a single ovum are termed *uniovular*, and as they are invariably of the same sex, *homologous*. Conjoined twins are uniovular and in all the examples in whom the sex can be determined homologous.

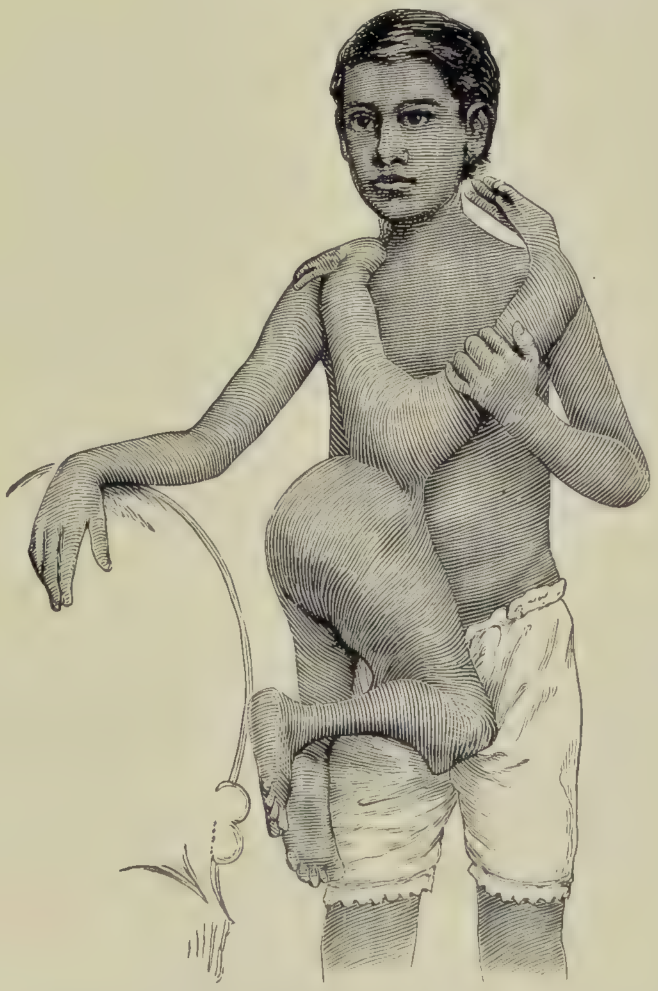

FIG. 220.—LALOO, A HINDOO WITH A PARASITIC FETUS ATTACHED TO HIS THORAX (Bland-Sutton "On Tumours").

When two embryos are conjoined, and one goes on to complete development, while only certain parts of its companion continue to grow, the result is a *parasitic fetus*. The mature individual supporting it is called the *autosite*.

In other examples the suppressed fetus consists of an irregular-shaped tumor growing, perhaps, from the posterior surface of the sacrum, or within the abdomen or thorax, which on dissection contains a few vertebræ, or processes of skin resembling digits, associated with a piece of intestine or an imperfect liver. This is a *teratoma*.

In order to demonstrate the relation between parasitic fetuses and teratomata, it will be useful to refer to dichotomy. In animals and vegetables there is a strong tendency for parts ending in free extremities to bifurcate or dichotomize. When this affects digits the result is supernumerary fingers and toes. Should it extend to the axis of the limb, supernumerary legs, wings, or fins are produced. Dichotomy is not confined to the limbs, but affects also the axis of the trunk. When the whole embryonic axis dichotomizes, twins are produced. Should cleavage be partial, and affect the caudal end of the trunk, it is spoken of as posterior dichotomy. When it involves the anterior end it is called anterior dichotomy. With complete dichotomy, in which both embryos go on to full development, either as separate or conjoined twins, we are not further concerned, and the conditions arising from the imperfect growth of one embryo while its companion continues to develop must be deferred until we have discussed the results of partial dichotomy.

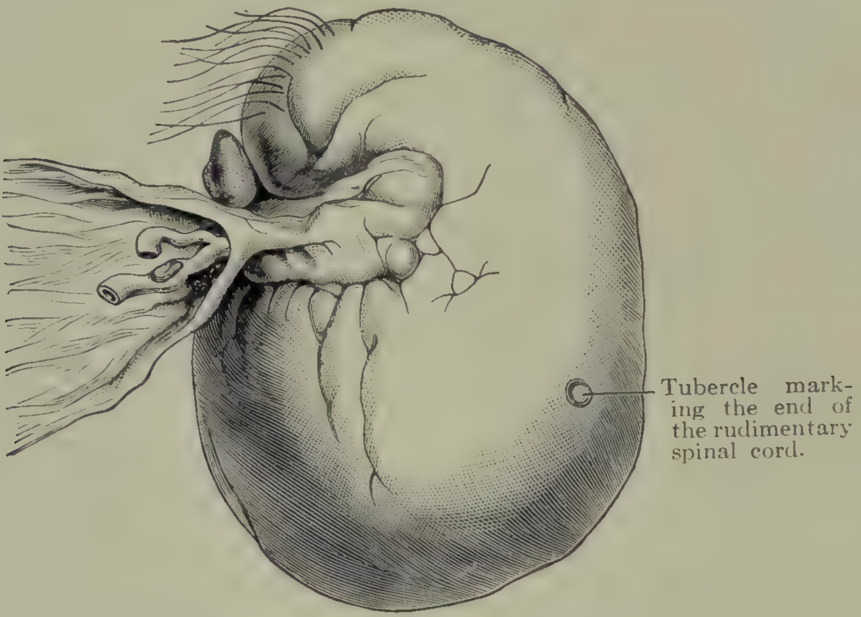

Fig. 221.—An Acardiac Fetus (Bland-Sutton "On Tumours").

Posterior Dichotomy.—When cleavage involves the caudal section of the trunk-axis to any serious extent it necessarily follows that the pelvis as well as the vertebral column will be duplicated; it is also obvious that the duplication of the pelvis involves a corresponding increase in the number of the pelvic organs, including the limbs. Thus it follows that supernumerary hind-limbs may arise from dichotomy affecting the embryonic limb, or from cleavage of the caudal end of the trunk. The two modes also hold good for duplication of the fore-limbs. The limbs may project from the ventral aspect of the pelvis, or be, as it were, dislocated on to the dorsal surface. Occasionally they occupy a position midway between these two extremes and lie more or less parallel with the normal hind-limbs.

In some individuals one pair of supernumerary limbs fuse throughout their length, and in others one limb is suppressed, but it is a noteworthy fact in its bearing on the cleavage theory that in all specimens of supernumerary limbs due to posterior cleavage there is an accessory but usually imperforate anus.

When the parasitic fetus is so suppressed as to form only a shapeless or deformed lump, then the mass would be called a teratoma.

It is a fact that the autosite has no power of initiating independent movements in the limbs of the parasite, nevertheless he can localize the prick of a pin on the parasite and feel uncomfortable when the parasite is cold, and involuntary movements may be produced in some teratomata by initiating them.

Anterior Dichotomy.—Cleavage may affect the facial portion only and produce duplication of the jaws, or it may involve the head and produce a two-headed individual. Should it extend to the thoracic region of the spine, then an animal with two heads and duplicated fore-limbs is the result. When partial dichotomy attacks the head, the median parts of the duplicated face are so conjoined and malformed that they project into the pharynx or are attached to its roof by a pedicle. Such tumors are called *basicranial teratomata;* the majority of tumors called pharyngeal dermoids are of this nature.

As a good example of the difficulty in interpreting the nature of tumors covered with skin and bearing teeth, the student should read the section *Heterotopic teeth* (p. 832). It is also instructive to find in a teratoma some one element of the mature form of the animal in an almost normal condition, such as a tooth or a vertebra, although the embryo is only represented by a mere fraction of the whole.

It is well to remember that the majority of suppressed fetuses of the parasitic variety when attached to the external parts of the autosite, though sources of great inconvenience to it, never in any serious way endanger life; it is otherwise when they are attached to the internal parts of the autosite and grow within the thorax or abdomen. This condition of things is discussed on page 844.

Teratomata of the Pharynx and Palate.—Considering the very distinctive features of a dermoid and a teratoma, it would scarcely be imagined that a tumor could come under observation in connection with the pharynx where there would be difficulty in deciding whether it was dermoid or teratoid.

It is noteworthy that the regions in relation with the cephalic as well as the caudal termination of the notochord are common positions for teratomata, and a great deal of the confusion which formerly encompassed the nature of those masses, generically classed as congenital sacrococcygeal tumors, in a measure surrounds congenital tumors of the pharynx and palate. The matter is rendered more difficult by the complex development of the palate.

Dermoids of the palate and naso-pharynx usually take the form of pedunculated skin-covered tumors. The central part of the tumor consists of a solid core of connective tissue, hyaline cartilage, and a variable amount of striped muscle-tissue. The skin is usually beset with hair. A dermoid of this kind is always congenital, rarely large, and in many cases it is difficult to decide whether the tumor grows from the palate or from the base of the skull and projects through the gap in the bony palate. Sometimes the attachment is so slender that the dermoid undergoes spontaneous detachment; in one instance the child swallowed the tumor and voided it next day by the anus (Lambl). Occasionally the tumor is sessile, and may even project into the floor of the pituitary fossa and compress the optic nerves and tracts.

Windle has collected the literature relating to dermoid and teratoid tumors of the pharynx under the title of *Epignathus*, and has summarized the various views in regard to the nature of this condition. It is noteworthy that pedunculated skin-clad and pilose tumors are only found in the naso-pharynx and rectum (see p. 827); in each situation they sometimes possess one or more teeth.

In describing teratomata care was particularly taken to emphasize the fact that many cases of duplicity of parts depended on dichotomy. Cleavage may be so slight at the cephalic end of the embryo as only to involve the face or even the jaws. Of this I have described several specimens, which make it clear that an identical state of things takes place in connection with the jaws as with the pelvic limbs. When this is the case, the supernumerary maxillæ fuse together and are impacted in the naso-pharynx and fixed to the base of the sphenoid. I have examined a large number of specimens (many of which are preserved in the splendid Teratological Collection of the Museum of the Royal College of Surgeons), in which every gradation is traced, from well-formed maxillæ with unerupted teeth to a confused lump of teeth, bone, and cartilage impacted in the palate, but firmly united by a broad base to the sphenoid in the neighborhood of the pituitary fossa.

In one remarkable case of a double pig in which two pigs were conjoined by the lateral aspects of their heads, I found every part duplicated except the mandibles. This led me to make a careful examination, and on dissecting the pharynx I found the missing mandibles hanging in the pharynx as a teratoma growing from the under surface of the basi-sphenoid.

Treatment of Teratomata.—Parasitic acardiacs are in almost all cases so extremely valuable as sources of gain in fairs, shows, and large cities that the parents, or the unscrupulous individuals who get possession of these children, will not permit operative interference. When the parasitic acardiac is of the amorphous variety and attached to the dorsal surface of the sacrum, attempts may be made to remove it.

In pre-antiseptic days the child rarely survived the operation, but in recent years better results have been obtained, especially in regard to sacral teratomata.

In one remarkable case of xiphiopagous twins, Radica and Doodica, one of them became the victim of tuberculous peritonitis, and Doyen divided the uniting band; the tuberculous twin died six hours after the operation, the other survived.

Dermoids.—*Dermoids are tumors furnished with skin occurring in situations where this structure is not found under normal conditions.*

In its simplest condition a dermoid has the form of a more or less globular sac or cyst; its inner wall is lined with stratified epithelium furnished with hair and sebaceous gland, and often with sweat glands. The shed hair, epithelium, and the excretion from the glands accumulate within the sac and slowly distend it.

Dermoids of this simple character form two genera according to their mode of origin. The most frequent situation for dermoids is in the lines where during early embryonic life coalescence takes place between cutaneous surfaces. These are known as *sequestration dermoids.*

The rarer kind arise in what are known as obsolete canals, and are in consequence known as *tubulo-dermoids.*

Dermoids belonging to these genera occur only on the head, neck, and trunk.

Sequestration Dermoids.—These tumors occur strictly in the regions of the embryonic fissures and are due to the inclusion of surface epithelium. They are common on the face in the lines of the facial fissures, and are frequently seen at the inner and outer angles of the orbit, in the upper eyelid, in the course of the naso-facial sulcus, in the middle line of the chin, and on the nose.

In the trunk dermoids arise in the regions where the lateral halves of the body coalesce. This line of union begins below the occipital protuberance and extends along the middle of the back to the coccyx; it then passes through the perineum (scrotum in the male), and upwards through the umbilicus, thorax, neck, and chin, to terminate at the margin of the lower lip.

Dermoids of the back are sometimes associated with spina bifida, and occasionally it is difficult to decide clinically between a spina bifida sac, a meningocele, and a dermoid. More rarely a dermoid will extend deeply between the vertebral arches, and pressing on the spinal cord produce paraplegia.

Dermoids of the scrotum are rare and must be sharply distinguished from those arising in connection with the testicle. The tunica vaginalis is a sharp boundary.

Dermoids of the Scalp and Dura Mater.—The common situations for dermoids of the scalp are over the anterior fontanelle (bregma) and the occipital protuberance. In these situations they are occasionally confounded with sebaceous cysts or with meningoceles. Dermoids of the scalp often have a thin pedunculated attachment to the dura mater, the pedicle traversing a hole in the underlying bone, unless the cyst is over a fontanelle. The term "wen" used to be applied indifferently to sebaceous cysts and dermoids of the scalp.

Although at first sight a dermoid connected with the dura mater and projecting into the brain seems to violate all embryologic rules, nevertheless, when we view this membrane from a morphologic standpoint, a satisfactory explanation is forthcoming.

Morphologically considered, the bony framework of the skull is an additional element to the primitive cranium, which is represented by the dura mater; the term extracranial should strictly apply to all tissues outside the dura mater. In surgical practice we find it convenient to regard the bones as the boundary of the skull, but morphologically this is inaccurate; the skull-bones are secondary cranial elements. Early in embryonic life the dura mater and the skin are in contact; gradually the base and portions of the side-walls of the membranous cranium chondrify, thus separating the skin from the dura mater. In the vault of the skull, bone develops between the dura mater and its cutaneous cap, but the skin and dura mater remain in contact along the various sutures even for a year or more after birth. This relation of the dura mater and skin persists longest in the region of the anterior fontanelle (bregma) and the neighborhood of the inion. Should the skin be imperfectly separated, or a portion remain persistently adherent to the dura mater, it would act precisely as a tumor-germ and give rise to a dermoid. Such a tumor may retain its original attachment to the dura mater, and its pedicle become surrounded by bone; the dermoid would lie outside the bone, but be lodged in a depression on its surface, with an aperture transmitting its pedicle. On the other hand, the tumor may become separated from the skin by bone; it would then project on the inner surface, or between the layers of the dura mater. If this view of the origin of dermoids of the scalp be admitted, we must then modify our teaching, and say that the depressions in which dermoids of the cranium are lodged arise as imperfections in the developmental process, and are not due to absorption induced by pressure; further, the fibrous connection of such dermoids with the underlying dura mater is primary, not accidental.

The relation of dermoids to the tentorium requires further consideration. A study of the development of the tentorium cerebelli will demonstrate that it is composed of two folds of dura mater, and it arises as an infolding or crease in this membrane, caused by the rapid backward extension of the developing cerebrum. The opposed surfaces of the tentorial lamellæ, like the outer surface of the dura mater in relation with the cerebrum, were originally in contact with the skin, and as the posterior margins of the bay or recess formed by the crease in the dura mater come together, a portion of the skin may become nipped or even sequestrated between the layers of the tentorium; this, preserving its vitality, and in some cases its cutaneous connections, may ultimately give rise to an intracranial dermoid.

There are some careful descriptions of dermoids which were found lying on the inner aspect of the dura mater and without any connection with it; and in some of the cases the tumor was embedded in the substance of the cerebrum, and in more than one instance it is stated that they were connected with choroid plexuses of the ventricles.

It is difficult on any current theory of dermoids to account for their origin in such situations.

Some complex tumors found in the neighborhood of the sella turcica and described as dermoids are teratomata. Dural dermoids are carefully considered by Bostroem.*

Dermoids and cysts arising in the branchial folds and in connection with the thyroglossal duct will be considered in the chapters devoted to the neck and tongue.

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* "Centralbl. f. allgemeine Pathol. u. patholog. Anat.," Jena, January, 1897.

Implantation Cysts.—These small cysts should not be included among tumors, but their consideration is imperative in connection with sequestration dermoids, for they furnish valuable evidence that dermoids of this genus arise from "rests," the result of faulty coalescence.

These cysts are caused by the accidental implantation of portions of skin, epithelium, or hair bulbs in the underlying connective tissues. The transplanted tissue acts in many instances as a graft, and forms a small cyst. Implantation cysts have received a variety of names, such as dermal cysts, traumatic dermoids, sebaceous cysts of the fingers, etc.

They are common on the fingers, the cornea, and the iris, but they may arise on any part of the skin.

Implantation cysts vary much in size; some are scarcely as big as a split pea, others may be as large as a ripe cherry. In many the microscopic characters "appear as if a piece of the skin covering the pulp of the finger had been inverted" (Shattock). In others the implanted epidermis seems to have been shed in layers, so that on section the interior of the cyst is occupied by epithelial laminæ. When these cysts occur on the scalp, they contain hair.

Implantation cysts are caused in a variety of ways, such as punctures by awls, forks, needles, thorns, glass, etc.; also accidental wounds by knives, incisions by scalpels, bites and lacerations.

Iritic Cysts.—Cysts of the iris are of comparative rarity, generally appearing as transparent vesicles situated on its anterior surface. As a rule, they are sessile, but occasionally they possess a pedicle. The contents may be opaque, but in exceptional cases they have been filled with sebaceous material, such as fills the cavities of dermoids. It is now recognized that these cysts are due to fragments of corneal epithelium, epidermis, and eyelashes carried into the anterior chamber by accident.

Numerous instances are known in which eyelashes, sometimes as many as six, have been implanted on the iris by foreign bodies penetrating the cornea, such as knives, needles, foils, and swords. Similar cysts have been produced in the eyes of rabbits by the artificial introduction of eyelashes and epithelium into the anterior chamber.

Corneal Cysts.—In addition to the evidence furnished by implantation cysts of the iris, we know that similar cysts occur in the cornea. Treacher Collins has investigated this matter, and has published some valuable researches in which he has succeeded in demonstrating that after gunshot injuries of the eyeball, blows from tip-cats, and incisions made for the extraction of cataracts, cysts, usually of small size, are liable to form in the cornea near the seat of injury. In some of the specimens the cyst may be very large and conspicuous; when examined microscopically, their inner walls are found lined with layers of cells identical with those covering the anterior surface of the conjunctiva. The structure of these cysts, taken in conjunction with the antecedent injuries, thoroughly supports the view that they arise from conjunctival epithelium transplanted into the deep tissues of the cornea.

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Teratomata and Dermoids Connected with the Rectum.—In order to appreciate the nature of dermoids arising in the immediate neighborhood of the rectum, it will be necessary to consider a few points connected with the embryology of this portion of the alimentary canal. In the early embryo the central canal of the spinal cord and the alimentary canal are continuous around the caudal extremity of the notochord. This passage, which brings the developing cord and gut into such intimate union, is known as the neurenteric canal. When the proctodæum invaginates to form part of the cloacal chamber it meets the gut at a point some distance anterior to the spot where the neurenteric canal opens into it; hence there is for a time a segment of intestine extending behind the anus, and termed in consequence the "post-anal gut." Afterward this post-anal section of the embryonic intestine disappears. There is good reason to regard the post-anal gut as the source of that variety of congenital sacrococcygeal tumor which was named by Braune and several writers who followed him "congenital cystic sarcoma." These will be referred to as tumors of the *post-anal gut.* In addition, it will be necessary to consider dermoids situated between the rectum and the hollow of the sacrum—*post-rectal dermoids;* and certain pedunculated tumors situated within the rectum—*rectal dermoids.*

Tumors which arise in the post-anal gut exhibit a definite structure; they are composed of closed vesicles lined with glandular epithelium, and contain glue-like fluid. Many of these tumors are composed of cysts and duct-like passages lined with cubical epithelium, held together by richly cellular connective tissue. In many situations the epithelium is columnar, set upon flatter cubical cells. The cysts are filled with ropy mucus, and vary in size from a nut to the smallest space visible to the naked eye; many contain intracystic processes. These tumors present such very definite characters that they are sure to attract attention, and when large size makes them very conspicuous.

Middeldorpf was the first to associate clearly a congenital sacrococcygeal tumor with the post-anal gut. His specimen was removed from the neighborhood of the anus of a girl a year old. The tumor contained connective tissue, mucous membrane with characteristic follicles, submucous tissue, longitudinal and circular layers of muscle fibers. I had come to the same conclusion in regard to the probable origin of these tumors before the publication of Middeldorpf's paper; his case is the most conclusive on record.

Post-rectal dermoids are very rare, and do not form such large projecting masses as the preceding species. In many instances they are not noticed until after infant life, and their clinical tendencies are of a different character. It is also somewhat remarkable that dermoids, although they are met with in many parts of the body, contain teeth only in certain situations. The post-rectal region comes into this category (Fig. 222).

Such dermoids also occur as surgical surprises, especially when they attain very large dimensions and extend upward behind the pelvic peritoneum of men and women. Ord recorded a remarkable case which occurred in a man twenty-eight years old; the dermoid weighed fourteen pounds. Page successfully removed a dermoid, weighing three pounds, which occupied the hollow of the sacrum in a woman of forty-seven years; it lay behind the rectum. The pultaceous matter was evacuated through an incision in the perineum; the cyst wall could then be easily enucleated.

Skutsch has recorded two examples of post-rectal dermoids and collected the chief German cases. One of the records is interesting from the fact that the patient was pregnant, and the operator was able to empty and partially enucleate the dermoid through an incision in the perineum without disturbing the pregnancy.

Post-rectal dermoids sometimes open spontaneously in the perineum; the fistula is usually situated in the middle line of the perineum near the tip of the coccyx. Keen removed a post-rectal teratoma from a girl aged three and one-half years; in the middle there was a fistulous opening which led upward to the third piece of the sacrum. Professor Coplin found that the tumor contained fat, cartilage, etc. The tubular tract resembled a trachea, was lined with ciliated epithelium, and possessed imperfect cartilaginous rings.

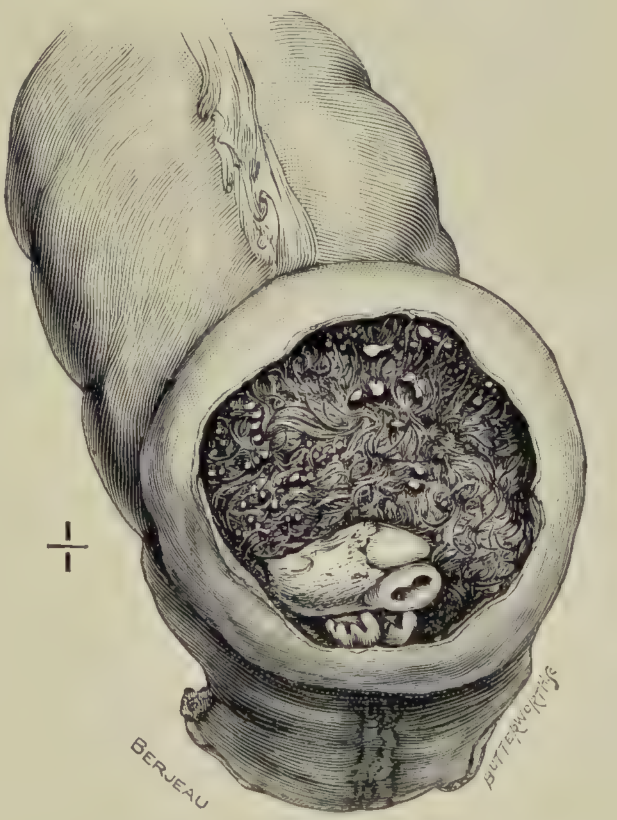

FIG. 222.—A POST-RECTAL DERMOID WITH HAIR AND A TOOTH (Museum Middlesex Hospital).

Rectal Dermoids.—Several examples of dermoid tumors have been described growing from the mucous membrane of the rectum; a curious feature in these cases is that the tumors are furnished with long locks of hair, which protrude from the anus and annoy the patients. Like post-rectal dermoids, they sometimes contain teeth.

Pedunculated rectal dermoids annoy the patients by protruding at the anus after defecation. When seated in the upper region of the rectum they may cause invagination of the bowel, producing the signs of intestinal obstruction. In one reported case the woman was troubled with the long hairs which protruded at the anus and she used to pull them out with her hand (Danzel). Moynihan removed one from between the layers of the meso-sigmoid of a woman; she also had a dermoid in the connective tissue of the pelvis. Her ovaries were healthy.

Treatment.—This is very simple, as the stalk of the tumor only needs transfixing with a ligature, and after securely tying the dermoid is cut away.

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Dermoids (Embryomata) of the Ovary.—The human ovary consists morphologically and anatomically of three distinct parts: The oöphoron, the paroöphoron, and the parovarium (epoöphoron) (Fig. 223).

The oöphoron or egg-bearing portion of the ovary concerns us in this section, for it is the region of the ovary in which dermoids arise. The cysts which must be considered under this heading are of three varieties and will be considered separately under the following headings: Simple cysts, adenomata, and dermoids.

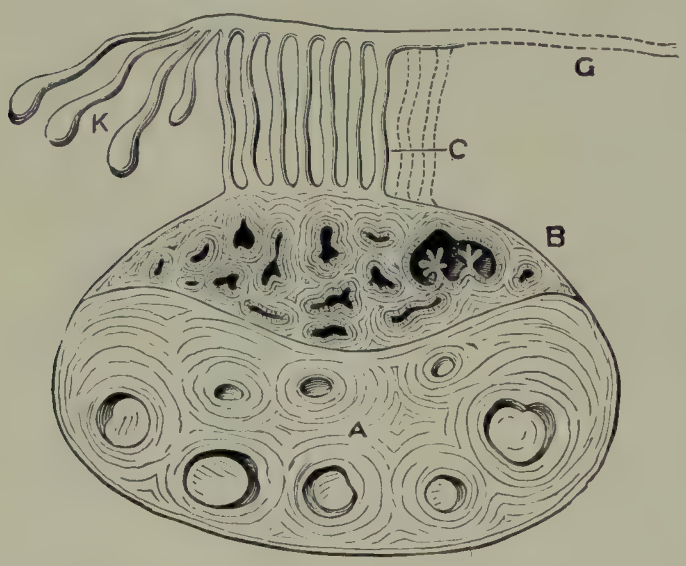

Fig. 223.—Parovarium (Semi-diagrammatic).
A, Oöphoron; B, paroöphoron; K, Kobelt's tubes; C, vertical tubes of the parovarium; G, Gärtner's duct (from Bland-Sutton "On Tumours.")

Simple Cysts.—These may be unilocular or multilocular. A small oöphoronic cyst is an enlarged ovarian follicle, and its walls are furnished with a well-developed membrana granulosa. In a very early stage it is easy to demonstrate the relation of such a cyst to the oöphoron. As the cyst enlarges it causes rapid absorption of the paroöphoron, and the region in which it arose is then not so easily demonstrable. Small, thin-walled, transparent cysts sometimes arise in corpora lutea.

In cysts containing three or four liters of fluid the walls will be found to consist of fibrous tissue, and the epithelium is rarely detected. It is impossible to state definitely the size of a cyst in which the epithelium disappears. The absence is due to atrophic changes, the consequence of the continual pressure exerted by the accumulating fluid. Precisely similar changes may be studied in the mucous membrane of greatly distended gall-bladders. In large multilocular cysts, although the big loculi may be destitute of epithelium, the smaller cavities will retain their epithelium, which may be columnar, cubical, or stratified.

An extremely simple means of determining an oöphoronic tumor is to note the relation of the Fallopian tube; it lies curled up on the cyst, and when the parts are stretched the tube and tumor are separated from each other by the mesosalpinx.

Adenoma.—This is not only an important but an extremely interesting tumor. As a rule, it has a dense fibrous capsule, and its surface is frequently lobulated. Such a tumor attains great dimensions and is often composed of innumerable cysts which vary in size from a cavity no bigger than a pea to one with the capacity of a liter or more. The walls of the smaller cavities and loculi are lined with rich columnar epithelium and often contain mucous glands. The fluid contained in the loculi of ovarian adenomata is identical in its physical and chemical characters with mucus. Occasionally it is as thick and tenacious as jelly. The tissue lining the cavities is in many specimens indistinguishable from mucous membrane.

The epithelium lining the loculi of ovarian adenomata sometimes attains extraordinary proportions. The largest columnar cells I have ever seen occurred in these tumors, excelling those remarkable cells in the glandular spaces of rectal polypi occasionally found in children. The translucency of the cells is due to the mucus they contain. The source of these large cells is undoubtedly the epithelium lining the ovarian follicle.

In some specimens of ovarian adenomata the secondary loculi give rise to projections on the periphery of the tumor; when numerous and close together, these projections cause the tumor to resemble a colossal bunch of grapes. It is no uncommon thing for a loculus of an ovarian adenoma to burst into the belly. When this happens the mucus which escapes is tolerated, but not absorbed, by the peritoneum. When the rent in the loculus is not repaired the glands in its walls continue to secrete, and the mucus accumulates in the belly, simulating hydroperitoneum.

Dermoids.—A very large proportion of oöphoronic cysts contain skin or mucous membrane, or both these structures, and some of the many organs peculiar to them, such as hair; sebaceous, mucous, and sweat glands; dermal bone, horn, nail, nipples, and mammæ; teeth also occur in great numbers. Such are called *dermoids*. They may be multilocular or unilocular, and attain a weight of 20 or even 40 kilograms. Sometimes a cyst will be lined throughout with typical mucous membrane covered with regular columnar epithelium, and will contain mucous glands.

The contents of a dermoid usually consist of a pultaceous mixture of shed epithelium, fat, and loose hair. In many complex multilocular dermoids some of the loculi contain mucous membrane and are filled with mucus; others possess hairs; and a few may be quite barren.

Cysts occur in the oöphoron at all periods of life, even in very young children, and I have collected records of over one hundred cases in girls under fifteen years of age in which ovariotomy was a necessity from the size of the tumor. In one remarkable case an ovarian tumor removed from a girl fifteen years of age weighed 44 kilos. The girl without the tumor weighed 27 kilos (Keen).

Adenomata and dermoids are very apt to affect both ovaries simultaneously; very rarely two independent dermoids may arise in one ovary, and it is a fact that both ovaries may be so distorted and destroyed by dermoids that the true ovarian tissue is unrecognizable to the naked eye, yet these organs are able not only to dominate menstruation but to discharge their egg-bearing functions successfully.

The cutaneous and other epithelial structures found in ovarian dermoids present such extraordinary variation as to demand some notice.

In the first place, it is necessary to point out that the complex structures in these dermoids are localized to a definite area of the cyst wall; the inferences to be drawn from this will be considered later.

Skin.—This, in some specimens, is very thick, but it rarely possesses papillæ, and these when present are not furnished with touch corpuscles. Pigment is occasionally observed in the deep layer which would correspond to the rete mucosum. An epidermis may be demonstrated; sometimes it is very thick and the superficial layers are shed into the cavity of the dermoid in broad flakes. The usual arrangement of the epithelium resembles that which is found on the buccal mucous membrane rather than on skin in general. The subcutaneous tissue of dermoids is often particularly rich in delicate fat.

In a few instances the epidermis has been found transformed into *nail.* An ill-formed nail has been detected at the extremity of a piece of bone resembling a phalanx by several observers.

Hair.—This varies in length, color, and amount. A single tuft coiled into a ball and mixed with sebaceous matter is not infrequent, and may attain a length of 1.5 meters (Mundé). Frequently only a few hairs are found scattered on the cyst wall, or the hair may be rolled into balls and lie free in the cyst. Occasionally the shed hair will "felt." The color is equally capricious, and, as a rule, differs from that on the exterior of the individual. The hair in such cysts changes in color with age, and in elderly persons becomes quite white and is eventually shed, so that these cysts become actually bald. In an ovarian dermoid from a mare the hair resembled that on the animal's mane or tail. A similar tumor from an ewe contained wool.

Sebaceous Glands.—These exist in extraordinary abundance and are of large size; they are occasionally transformed into cysts and horns sprout from them.

Sweat Glands.—These are not so common, and usually form isolated clusters. I have not detected the characteristic twist of the duct so constant in normal sweat glands.

Thyroid Gland.—In 1893 I removed a large dermoid from a woman fifty years of age and detected in it a firm, rounded, encapsuled body as big as a walnut. The cut surface so closely resembled a thyroid gland that I examined it microscopically. It was composed of vesicles filled with colloid material and lined with the subcolumnar epithelium like the normal gland. Other observers have since recorded a like experience.

Pultaceous Material.—The cavities of ovarian dermoids are often filled with a semi-fluid mixture of epithelium, sebum, fat, shed hairs, and often cholesterin. In small cysts the sebum is sometimes so pure as to be quite white in color.

The fat may be liquid at the temperature of the body, but solidifies after its removal. In some dermoids it occurs in lumps of the density and color of cacao-butter. This variation probably depends on the proportion of stearin in the fat. In rare instances the shed epidermis forms rounded pill-like bodies or epithelial balls. In one specimen I found 3930 of these bodies. Epithelial balls occur in dermoids of the scalp and neck.

Ovarian Mammæ and Teats.—It is quite common to find in the interior of ovarian dermoids one or more tags of skin resembling a nipple or teat associated with hair and teeth. These teats may be small and inconspicuous, but, as a rule, they are obvious even to the most casual observer Often they are attached to rounded skin-covered prominences resembling mammæ. These teat-like processes of skin are imperforate and beset with large sebaceous glands. In some specimens the mamma is plump and well-formed, but consists of fat covered with skin; the nipple may even be surrounded by an areola; such are called *pseudo-mammæ.* Complete forms are sometimes found possessing glandular acini ducts, a perforated nipple, and furnish a viscid fluid which exhibits the microscopic characters of milk and contains colostrum globules. Teat-like processes of skin and pseudo-mammæ are found in intrathoracic dermoids (see p. 843).

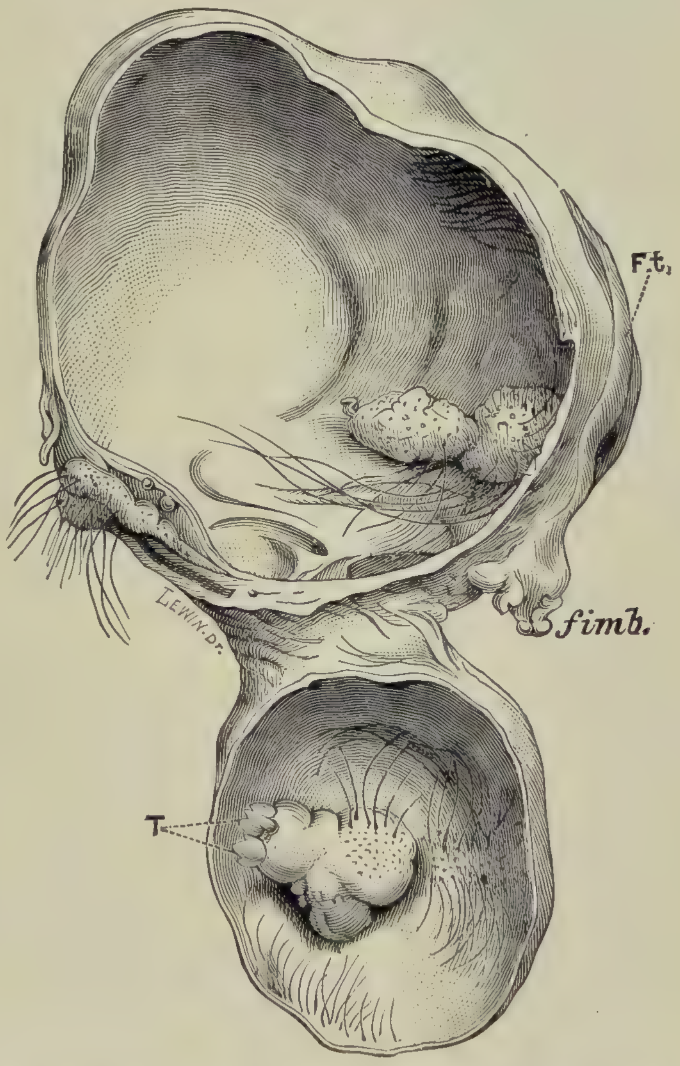

FIG. 224.—AN OVARIAN DERMOID (EMBRYOMA) WITH THREE LOCULI, EACH CONTAINING A TEAT OR NIPPLE (from Bland-Sutton's work on "Tumours").

Teeth.—Ovarian teeth are described in a special section (Heterotopic teeth, see below.

Epithelial Pearls.—The common form of epithelial pearl consists of concentric laminæ of horny epithelium. The central portions in some specimens are structureless and transparent like horn; in others the cells are large and distinct. Sometimes the epithelium forms onion-like layers without any tendency to cornification. The common mode by which pearls are formed is by the retention and subsequent molding of shed epithelium in the recesses of sebaceous glands, in mucous crypts, or in the folds of epithelial surfaces. Some are probably formed on the principle of enamel organs.

Bone.—This tissue is often present in ovarian dermoids in shapeless masses resembling the alveoli of jaws, or as irregular plates of extremely dense bone, "similar to the facial bones of an osseous fish" (Doran). Those writers who believed that dermoids were due to parthenogenesis saw in these ill-formed pieces of bone jaws, skulls, pelves, limbs, etc., and other skeletal elements, as their fancies led them. Rarely the fibrous capsule of a dermoid becomes calcified in flakes until a hard shell is formed.

Nerve-tissue.—Our knowledge in relation to nerve-tissue in ovarian dermoids is not very satisfactory. Several observers have detected the presence of tissue which in its histologic characters was indistinguishable from "cerebral matter." In several cases the brain substance was enclosed in a firm capsule, in structure like dura mater, lined with a delicate pia mater. The whole question of nerve-tissue in dermoids requires careful study, aided by the improved methods of staining now employed in neurologic histology.

In some of the malignant ovarian embryomata embryonic brain substance, neuroglia, and ganglion cells have been detected in the nodular dissemination on the peritoneum (Backhaus).

Heterotopic Teeth.—Among mammals the normal situation for teeth is the mouth (buccal cavity), but under pathologic and teratologic conditions they arise in such unexpected situations as the ovary, testis, rectum, neck, and pharynx in man, and in connection with the tympanum of horses (mastoid teeth).

Among heterotopic teeth those found in ovarian dermoids (embryomas) are the best known and have been the subject of several careful investigations.

Ovarian Teeth.—A large proportion of ovarian dermoids contain teeth. In number they vary greatly. Sometimes only two or three are found, in others twenty or more may be counted; a larger number is very unusual. The teeth may be embedded in loose ill-formed bone (Fig. 225) or project from a flat osseous plate like nails driven through a piece of thin wood. Often the roots of ovarian teeth are embedded in soft tissue, or the entire teeth remain hidden in crypts or cysts. When the crown projects boldly, the neck of the tooth may be surrounded with pink tissue resembling the gums.

Teeth occur more frequently in ovarian dermoids than would be gathered from the current descriptions. If the teeth are not actually erupted the surgeon may fail to notice them unless he makes, or orders to be made, a careful dissection of the dermoid. On several occasions I have astonished my assistants by directing a dermoid in which no dental structures were obvious to be destroyed by prolonged boiling; when the residue was examined many (sometimes twenty or thirty) teeth were found.

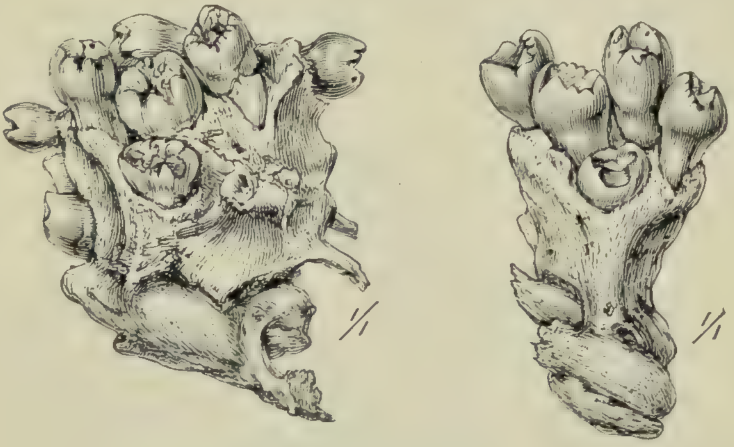

Fig. 225.—Cluster of Ovarian Teeth Embedded in Bone (Bland-Sutton "On Tumours").

The teeth are not scattered irregularly through the dermoid unless present in very great number, but are collected in one or more groups; they vary in shape and resemble incisors, canines, and supernumerary teeth. The root is usually single; teeth with more than one root or with a bifurcated root are very rare. When the crown is simple the root is long; multicuspidate teeth have short roots.

Ovarian teeth are composed of enamel and dentine; cementum is by no means constant. The enamel is lodged on the crown in lumps or hummocks, with deep ravines extending to the dentine. The enamel prisms run in all directions. The pulp is very irregular; some of the teeth, especially those resembling incisors and canines, may lack a central chamber. In multicuspidate teeth the pulp chamber is of fair size. In some the pulp is converted into osteo-dentine, in others it is full of fat globules. The presence of nerves in the pulps of ovarian teeth was asserted by Salter, and tissue resembling nerve-fibrils may be detected in pulp suitably prepared. Ovarian teeth develop on the same principle as normal teeth (Fig. 226).

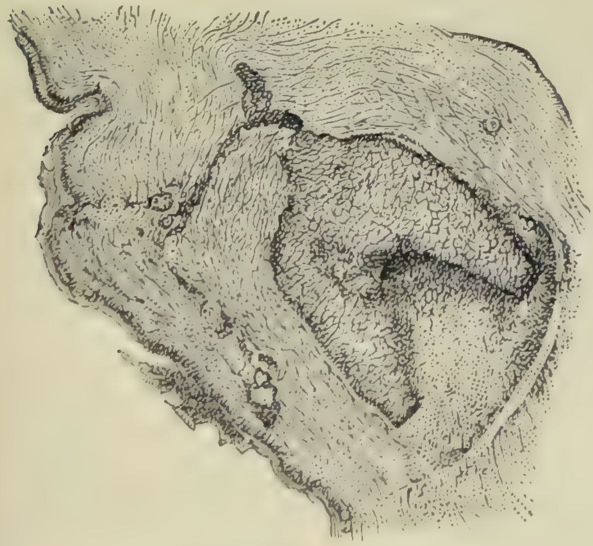

Fig. 226.—A Developing Ovarian Tooth Showing the Enamel-organ.
From an adult woman.

For several years I made a series of observations in order to determine if the development and eruption of ovarian teeth were in any way influenced by age, and to ascertain if, like the hair of dermoids, they were shed in old age. The evidence proved that the development of ovarian teeth is uninfluenced by age; for example, a dermoid the size of a tennis-ball, from a girl six years of age, contained many teeth, six of which were fully erupted, whereas an ovarian dermoid from a woman in middle life contained germs of teeth in great abundance, but none had reached the stage of calcification.

Mastoid (Tympanic) Teeth in Horses.—The occurrence of teeth in the mastoid portion of the temporal bone in horses has been known for upward of a century and specimens of these curious teeth exist in many veterinary museums.

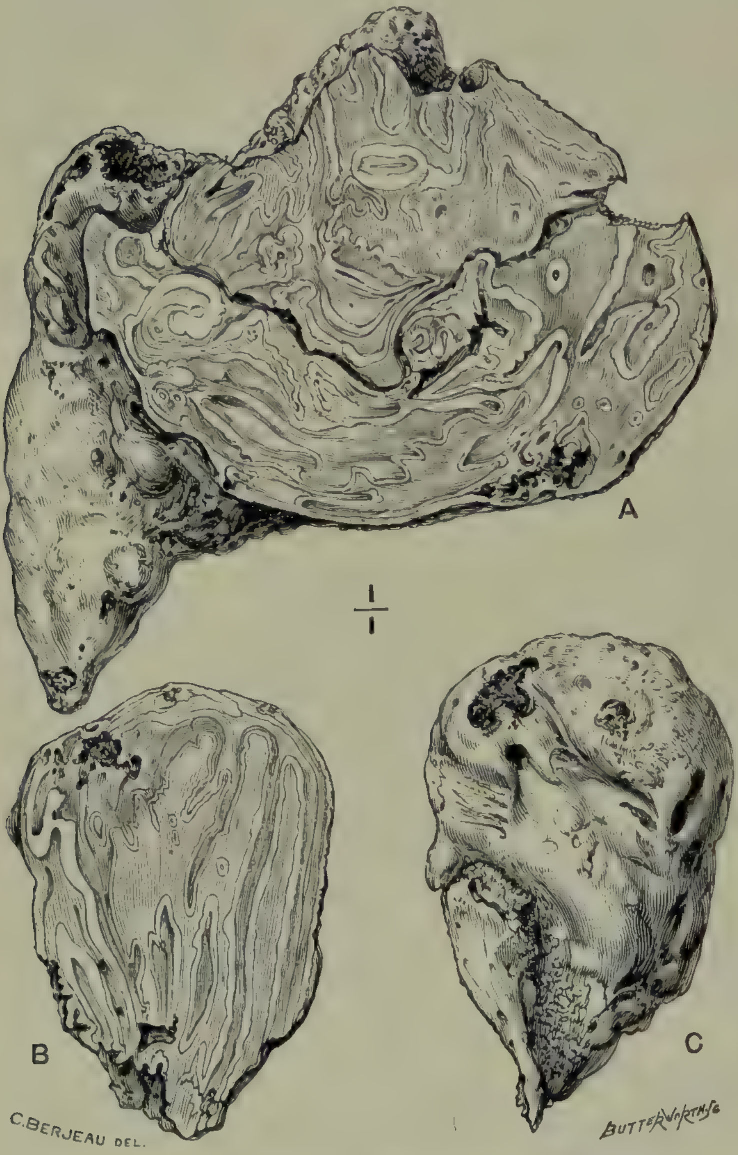

Fig. 227.—Mastoid Teeth from a Horse.

The number of teeth varies; as a rule, one tooth is present, stuck like a peg in the bone. It is not uncommon to find two and in rare instances four teeth.

Mastoid teeth are very misshapen and usually of the molar type; often they are such ill-formed lumps as to come under the denomination odontomes; indeed, Broca included these bodies among his *odontômes hétérotopiques*.

Mastoid teeth possess the three familiar dental tissues—enamel, dentine, and cementum. A careful examination of the very few available specimens in which the skull has been preserved with the mastoid teeth in position shows that they are in relation with the tympanum, and especially with that part of it known as the attic. This is true of a specimen in the museum of the Royal Veterinary College, London, in which a solitary tooth stands out from the remains of its bony capsules, the root of the tooth being lodged in the tympanic attic.

Owing to the kindness of Professor Dewar I was able to carefully study a skull with the teeth in position (Fig. 228). In this specimen the teeth are not lodged in sockets, but encysted by an incomplete bony capsule, in the mastoid portion of the temporal bone, especially in that part immediately overlapped by the squamosal. The cluster of teeth has markedly compressed the external auditory meatus. The tumor has deformed the interior of the cranium, and an uncovered portion of tooth projects into the cerebellar fossa. During life it was probably excluded by the dura mater. It is impossible to accurately determine the number of separate dental bodies in this specimen without destroying it, but I feel sure there are at least four separate pieces.

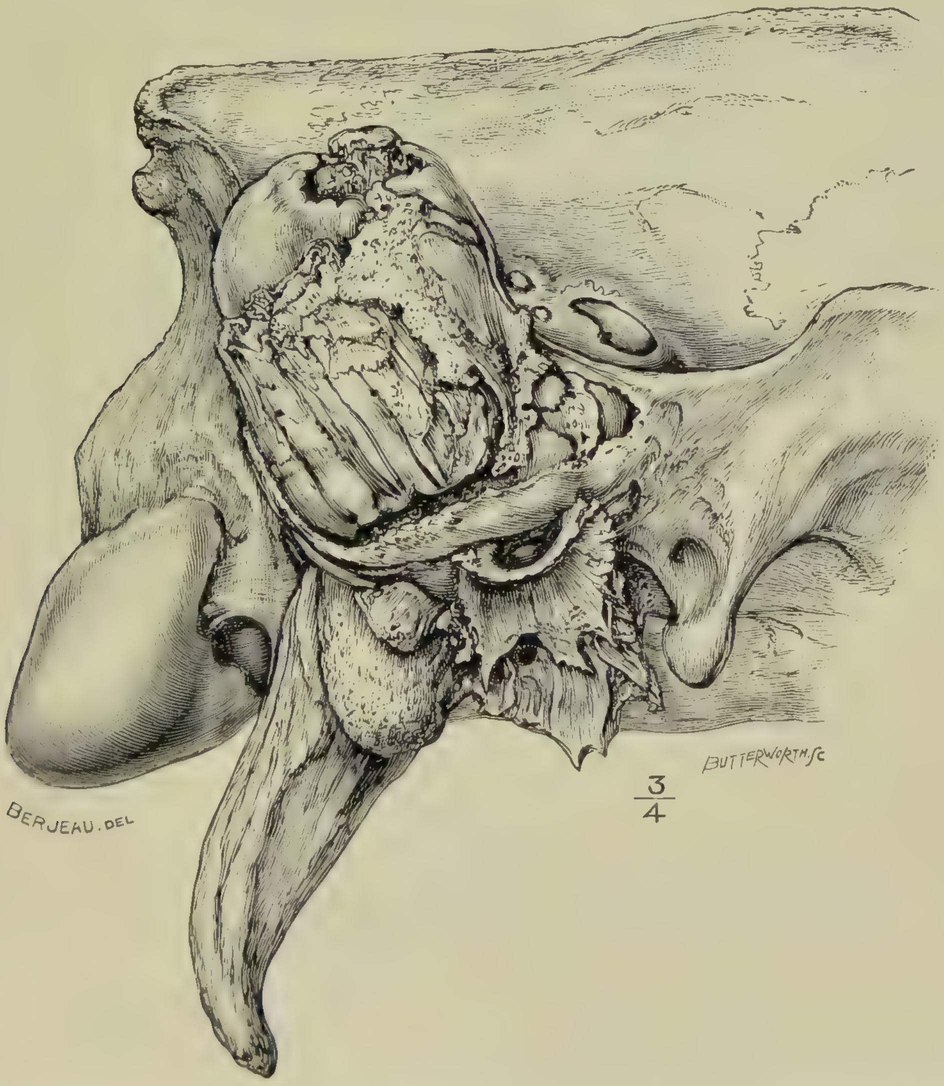

FIG. 228.—THE TYMPANIC REGION OF THE SKULL OF A HORSE WITH A CLUSTER OF MASTOID TEETH.

There is no satisfactory explanation available as to the origin of these teeth. There is, one would certainly imagine, some morphologic reason for their localization in the temporal bone, as well as their peculiar characters, for, as the drawings show, they have peculiarities in shape and size which should serve for their ready recognition, and enable us at once to distinguish them from testicular or ovarian teeth.

Before it is possible to make any decisive statement in regard to the nature of the mastoid teeth of horses, it is very desirable to obtain facts concerning their anatomic relationship with the soft parts, and especially the connection of the fistula with the pharynx.

Mastoid teeth are troublesome to horses and give rise to some interesting clinical conditions. The horse is usually brought to the veterinary surgeon on account of a swelling, but more frequently a sinus near the base of the auricle. When a probe is passed along the sinus it comes in contact with a tooth. The recorded cases of this disease fail to make it clear whether the sinus is congenital or is a consequence of suppuration as the tooth develops. The veterinarian usually treats these cases in a summary manner, for he enlarges the sinus and, ascertaining the exact position of the tooth, extracts it by forceps or by a chisel and mallet; he then stuffs the cavity with antiseptic gauze, and encourages it to become obliterated by granulations. A study of the character and position of these teeth shows that their removal is sometimes attended with difficulty, certainly with grave danger to the horse, and occasionally their extraction is impracticable. Cases are known in which horses have died from septic meningitis the result of suppuration around the teeth.

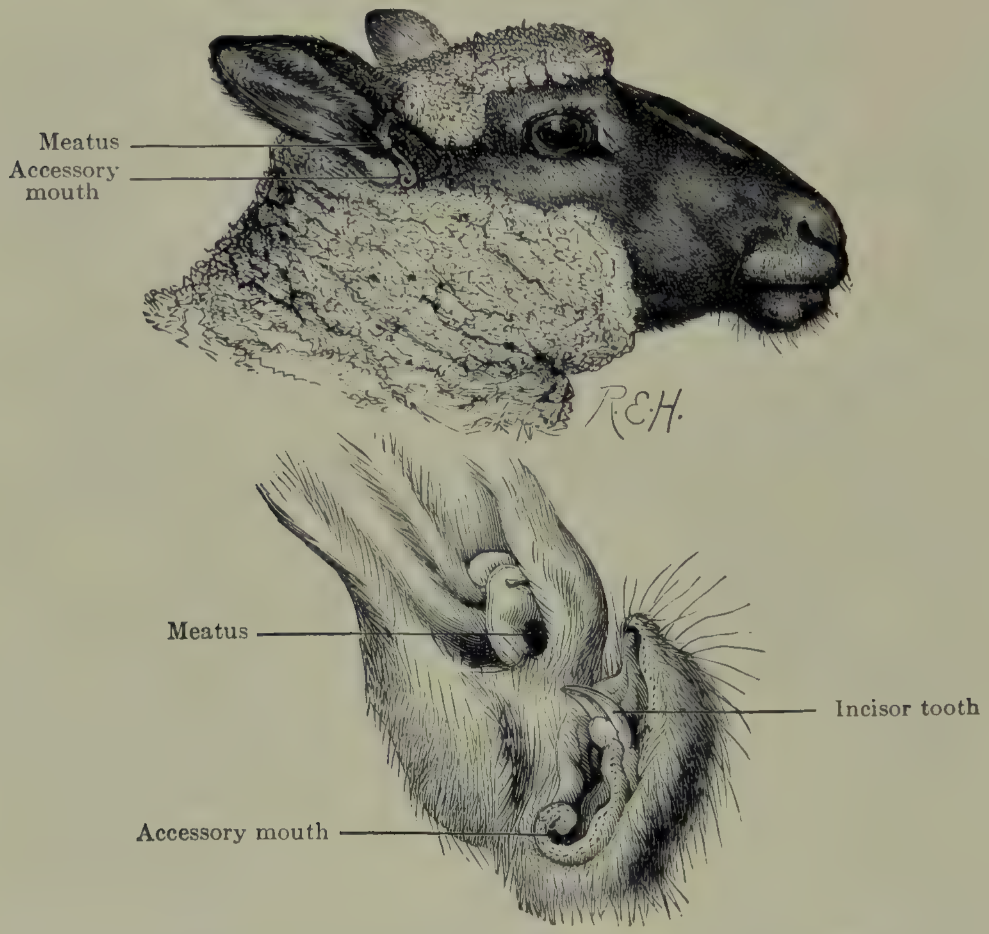

Fig. 229.—The Head of a Sheep to Show the Position of the Accessory Mouth. The lower figure represents the accessory mouth, tooth, gums, and lip of nearly natural size (from Bland-Sutton "On Tumors").

Cervical Teeth in Sheep.—Sheep are liable to a peculiar anomaly in the immediate neighborhood of the ear, which consists of a fistula opening near its base; but its skin edge is invariably surmounted by an incisor tooth. The first impression is that the opening represents a persistent branchial fistula, but in man teeth are not associated with these fistulæ. Congenital cervical fistulæ in sheep have received careful attention, and these investigations show that the abnormal orifice is an accessory mouth.

A good example which came under my notice is represented in Fig. 229; the tooth, which had the characters of a temporary incisor, is lodged in a bony pedicle surrounded by mucous membrane of the same features as the gums, and the cutaneous recess in which it is accommodated presents in the aspect which is in contact with the tooth a number of processes resembling the papillæ on the sheep's lips, and the arrangement of the wool on the outer surface of the accessory lip is identical with that covering its normal lip. This specimen by itself is somewhat puzzling, but a wider survey of the question adds a special interest to it.

Gurlt had the opportunity of studying several which enabled him to prove conclusively the nature of this condition, and in one of his specimens two temporary incisors were lodged in a miniature but unmistakable mandible, and associated with a tongue of corresponding size. The fistulous track communicated with the pharynx. Without entering too fully into the details of this matter, the revelation afforded by a careful anatomic study of the specimens amounts to this:

The cervical teeth and the associated structures are the remnants of an attached or parasitic fetus, and the cutaneous opening represents its mouth.

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The Nature of the Ovarian Dermoid (Embryoma).—It has been held by many writers during the last fifteen years, myself among the number, that dermoids of the ovary differ in so many respects from those found in connection with the embryonic fissures (sequestration dermoids) that they require separate consideration, not only from a taxonomic and anatomic point of view but also from genetic considerations. The old notion that they arise from included pieces of epiblast I have always endeavored to combat. Apart from all other considerations I have never ceased to urge that sequestration dermoids are congenital, whereas there is no authentic observation on record of a dermoid existing in an ovary at birth. It is quite true that they occur in infancy and early girlhood and are often of large size, and though I made a special and long-continued study of the ovaries of stillborn fetuses, and made unremitting inquiries among men who have specially interested themselves in this question, no specimen or record of such a condition is available. This at once establishes a distinction between the sequestration dermoid, the teratoma, and the so-called dermoid of the ovary; the distinctives may be expressed in this way:

1. A teratoma arises in the earliest period of embryonic life.
2. Sequestration dermoids arise in fetal life.
3. Ovarian dermoids (embryomas) are of post-natal origin.

In its simplest form an ovarian embryoma is indistinguishable from the common dermoid of the skin. It is a cyst lined with epithelium furnished with hair. In a more complex form it presents hair, teeth, sometimes in great number, secreting glands, and bone. In the most developed state there are organs, such as a piece of intestine, fragments of brain tissue, an unmistakable vulva and even an eye, a condition of things resembling the variety of fetal malformation known as an acardiac monster. This last form of ovarian dermoid is excessively rare.

It has been pointed out by Wilms that an ovarian dermoid presents two parts; namely, a cyst containing an embryonic rudiment. The cyst itself is made up of fibrous tissue arranged in wavy bundles; the inner aspect of the cyst wall is lined with loose connective tissue, and at one part it presents a skin-covered surface of variable extent, usually beset with hair. Associated with this skin-covered surface there is an "embryonal rudiment," usually in the form of a nipple-like process (pseudo-mamma). The amount of development of the "embryonal rudiment" varies greatly. It may be small and so inconspicuous as to be easily overlooked, or so large as to strike an eye usually unobservant. In rarer cases the "embryonal rudiment" approaches the complexity, so far as the presence of specialized organs are concerned, of the well-known acardiac fetus. Ovarian dermoids, however, do not always conform to this simple plan of construction; specimens occasionally come to hand which are composed of many loculi, and each loculus contains an embryonal rudiment; moreover, it is not uncommon to find more than one nipple-like process in a loculus. The interest of the painstaking investigation carried out by Wilms lies in the fact that the tissue underlying the skin-covered surface in the cyst often contains glandular tissue; occasionally this tissue is very abundant, and in a certain number of specimens the amount of glandular tissue is so large as to obscure the small cutaneous element it contains. Tumors of this kind are known as multilocular cysts, or multilocular glandular cysts; I have preferred, however, to speak of them as adenomata, in consideration of the enormous amount of gland tissue they contain, and pointed out in 1888 that these tumors should be classed with ovarian dermoids.

In order to account for these things there is an indication that some writers are inclined to revert to the theory which was very popular some years ago, and attribute the cysts to the imperfect development of an ovum, or parthenogenesis. This, however, will not explain matters, because one of the most distinguishing features of the dermoids which are found now and then in the thoracic cavity is the presence of a number of the nipple-like processes. Moreover, there is the difficulty of accounting for dermoid of the testis on this theory; and Orthmann has recently described an embryoma of the Fallopian tube possessing a tooth.

For many years I held the opinion that dermoids had never been found growing primarily from any abdominal viscus save the ovary, but in 1903 Mr. Arthur Hall sent me a specimen for examination in which a piliferous dermoid grew in the angle formed by the junction of the ileum and cecum between the layers of the peritoneum. The parts were removed after death from a man. It is difficult, on any of the theories adduced to explain the origin of tumors, to account for this dermoid.

It is worth noting that in 1799 Baillie, in regard to an ovarian dermoid containing pilose skin, suet, and teeth, observed that this change has been generally considered as the very imperfect rudiments of a fetus which has been formed in the ovarium. As, however, this change takes place in the ovarium before the uterus would appear capable of functions which would begin at the age of puberty, and where the hymen is entire, it is highly probable that it is independent of impregnation.

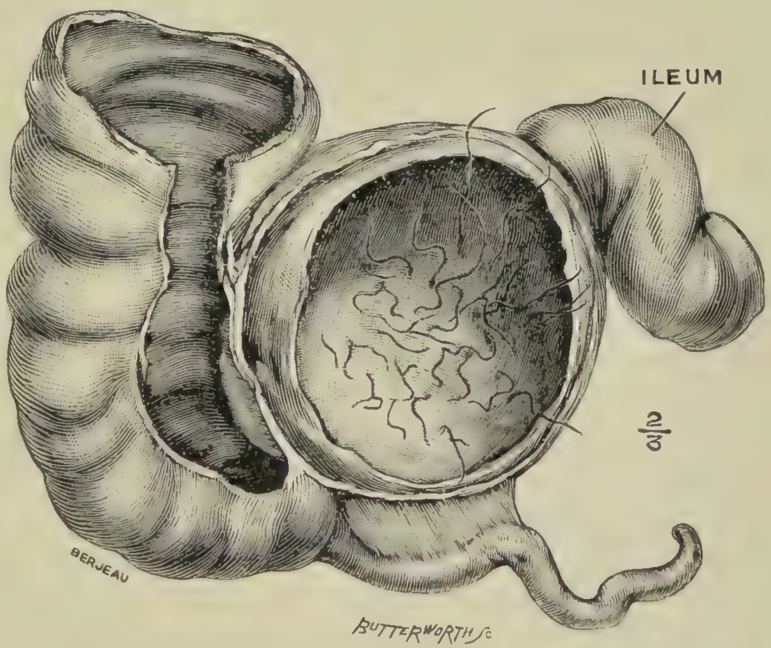

Fig. 230.—The Cecum and Adjacent Portion of the Ileum of a Man; a Dermoid Occupies the Angle between the Ileum and Cecum (from Bland-Sutton "On Tumours").

Interesting as all these questions are, the practical surgeon has now to face the important clinical fact that some of these ovarian teratomata display malignancy in its most dangerous form, namely, the power of dissemination. This will now be considered.

Malignancy of Ovarian Adenomata and Epithelial Infection.—If we restrict the term dermoid to those ovarian tumors which contain typical dermal elements, such as skin, hair, teeth, bone, sebaceous glands, and the like, it may be truly stated that they are the most benign tumors which attack women. There is, however, an interesting phenomenon connected with them which requires consideration. The details of at least five cases are available in which the peritoneum has been found dotted with minute knots furnished with small tufts of hair, or small dermoids growing among visceral adhesions even as high as the liver (Moore, Kolaczek, Fraenkel, Grawitz). In each of these cases there was a dermoid in the ovary, and in the clinical reports of some of these cases there was a distinct history of an injury to the abdomen. The facts available made it obvious that this singular condition could be explained by what I term epithelial injection, in which the contents of the dermoid escape into the belly and the epithelial elements are engrafted on the peritoneum and grow. This view is supported by what we know concerning detached fragments of the epidermis accidentally embedded in the subcutaneous tissue (see Implantation Cysts). If we widen the scope of the term ovarian dermoid and include the ovarian adenomata, which I contend is proper, then we have to include a rare variety of peritoneal infection which must clearly be considered malignant.

The most typical species of ovarian adenoma may infect the peritoneum. I removed from a woman fifty-one years of age a typical adenoma the size of a football. Two years later I removed an adenoma of similar size which had grown in the opposite ovary, but it had burst and the belly was filled with colloid stuff. Six years after the second operation this woman came under my notice with her belly enormously distended. On opening the abdomen it was found full of colloid, jelly; the whole of the parietal peritoneum, the uterine surface, the liver, intestines, and omentum were covered with clusters of small bodies amounting to many hundreds. These on microscopic examination exhibited the large columnar cells so characteristic of the adenomatous species of ovarian dermoid.

The patient to whom the above facts relate was alive and well three years after the operation.

In contrast to this the following facts are gloomy. I have records of three cases in which a tumor to the naked eye and on microscopic examination seemed to be a pure ovarian adenoma, but it had burst before removal and filled the belly with the viscous secretion. Before these patients recovered sufficient strength to leave their beds signs of recurrent growth made themselves obvious, and some twelve weeks later the patients died with multitudes of secondary nodules on the peritoneum.

Recently cases of this kind have been reported under the name of malignant embryomata. In some of them the peritoneal nodules contained cartilage, epithelial pearls, and ganglion cells. It has also been shown that the secondary nodules in many instances assume the form of grafts, and are in most instances confined to the peritoneum.

The whole bearing of the evidence at present available indicates that the more closely the embryonal elements of an ovarian embryoma conform to the adult tissues, the more benign will be its clinical course. The more widely the glandular elements depart from the normal type, the more prone will such elements be to infect peritoneum if they by accident or in the course of an operation become spread over the peritoneum.

My pathologic inquiries convinced me of the importance of these observations in 1890, and from that date I ceased to tap ovarian cysts in the course of removal; no matter what their size, I always endeavor to remove them entire, and have had no reason to regret it.

Carcinoma of the Ovary.—Primary cancer of the ovary is a rare disease and one concerning which we know little. We have come to learn that the ovaries are common situations for secondary cancer, especially when the disease arises primarily in the breast, gastro-intestinal tract, or the gall-bladder. In a fair proportion of patients both glands are infected, and in some instances the ovaries are so enlarged as to be obvious as tumors on physical examination.

Schlagenhaufer published a valuable inquiry showing the frequent association of malignant disease of the ovary with carcinoma of the stomach, intestine, and gall-bladder. In addition to some personal cases, he has collected a large number of recorded observations, making a total of 79 cases, and among these in 61 cases the primary focus was in the stomach, 10 in the bowels, and 7 in the gall-bladder or its associated ducts. The relation between the primary cancer and the masses in the ovary is demonstrated by the fact that the structure of the ovarian tumors varies according to the situation in the gastro-intestinal tract of the primary disease. In studying Schlagenhaufer's tables it is astonishing to find in what a large proportion of patients ovariotomy, unilateral or bilateral, had been performed and the primary cancerous focus in the stomach overlooked in spite of the presence of typical signs of gastric disturbance, especially persistent vomiting and progressive emaciation. This is an illustration of what may be called occupation bias, for the gynecologist would allow the presence of a definite tumor in the pelvis to occupy the foreground of the clinical picture.

The practical outcome of these observations is very important, and amounts to this: In cases of bilateral solid tumors of the ovary, if accompanied by vomiting and ascites, a careful and accurate examination should be made of the abdominal viscera, especially the stomach.

It is also significant that whenever surgeons have made inquiries into the remote results of ovariotomy, they have been astonished to find that many of the patients have perished from recurrence in the abdomen, or from intestinal obstruction. The fact that many solid tumors of the ovaries are metastatic offers an explanation of some of these unhappy sequences.

I have often been puzzled, on examining large deposits of cancer in the ovaries secondary to mammary or gastric carcinoma, to satisfy myself how these things come to pass. The riddle is, I think, solved by Handley's discovery of the mode in which mammary cancer involves the abdomen. He has demonstrated in a most convincing manner that cancer spreads by permeating the deep fascia; by an insidious process the cancer cells slowly creep along the lymphatics of the fascial plexus until they reach the epigastrium immediately below the ensiform cartilage; at this point the cancer-filled lymphatics of the fascial plexus in the middle line are separated from the subperitoneal fat only by a simple layer of fibrous tissue. Through this weak defence the cancer cells slowly find their way into the general peritoneal cavity and engraft themselves on the omentum and other suitable visceral plots, whereon they thrive and grow into metastatic nodules or lumps. Many of these infecting cells are conveyed into the pelvis and lodge on ovary, Fallopian tube, uterus, or pelvic peritoneum. The fluid normally present in the belly serves as an admirable vehicle for the transport of such cells, easily enabling them to reach the pelvic recesses, where they would remain undisturbed to grow into deadly lumps. If we apply Handley's observations on the serpiginous spread of mammary cancer, to a primary cancer in the stomach, gall-bladder, or colon, we may read its course in this way: Arising in the mucous membrane it slowly permeates it and implicates the submucous, muscular, and peritoneal coats; the cancer cells can then escape freely into the great serous cavity and be distributed by the fluid, aided by the movements of the bowels, and gradually reach the pelvis and other abdominal recesses. In the pelvis the most obvious organs on which they could fall would be the ovaries, as they so often rest on its floor. Under such conditions the ovaries may be fairly pictured in the mind receiving a covering of falling cancer-cells, as evergreen shrubs are clothed by snowflakes in winter.

The fact that other parts of the internal genitalia receive these cells is a matter of some importance, because one of the most striking features of operations for the removal of malignant ovaries is the rapidity with which the disease recurs. Lockyer made a valuable observation relating to this. He examined microscopically the tumors removed from bilateral carcinomatous disease, and although the attached tube and mesosalpinx belonging to each tumor appeared normal to eyes and fingers, when examined microscopically they were found extensively infected with cancer through the lymphatics.

Treatment.—The outcome of these pathologic observations will determine those who have to deal with bilateral malignant tumors of the ovaries to carefully examine the patient for evidence of primary cancer in the gastro-intestinal tract. If the disease is in such a position that it can be excised with good prospect of success, this may be done. Then it will be necessary to remove not only the infected ovaries, but the tubes, adjacent segments of the mesometria, and the uterus. Operations of this kind can be carried out with hopeful prospects only when there is no other evidence of gross infection than that afforded by the ovaries.

When the nature of solid malignant tumors of the ovaries comes to be more thoroughly appreciated by those who devote their attention to the surgery of the pelvic organs, it may enable them to contemplate the clinical aspect of the case with a wider knowledge of its surroundings and perhaps save themselves and their patients much acute disappointment.

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Internal Teratomata.—In a preceding section a brief description was given of the characters of parasitic fetuses and the more shapeless conglomerate teratomata representing suppressed fetuses attached to the external parts of otherwise normal individuals; attention was also drawn to skin-covered tumors which are occasionally found in the pharynx and in relation with the rectum. Suppressed fetuses and teratomata occur in the internal parts of the body,—the thorax and abdomen,—which in the degree of development equal those found on the external parts. They also run parallel with them in the other particular, namely, that they occasionally occur in the conglomerate form which makes it difficult to decide whether the tumor should be regarded as a teratoma or as a dermoid. The internal teratomata differ from the external kind, even in their most developed form, by the fact that they are enclosed in a cyst, and that the teratoma often imperils the life of the autosite from mechanical causes, and in some instances by displaying malignancy of a remarkable kind. It will be convenient to discuss the subject under three headings:

1. Intrathoracic teratomata.
2. Intra-abdominal teratomata.
3. Intracranial teratomata.

Intrathoracic Dermoids and Teratomata.—Dermoids within the thorax have been carefully studied by several writers. They are rare tumors, but cause very distressing consequences to the patients who are unfortunate enough to possess them. In the majority of instances they occupy the superior mediastinum and grow downward and to one or other side, compressing the lung. Occasionally the tumor is situated on the anterior face of the pericardium (Hale White). Many of the cases have been recorded as examples of "dermoid of the lungs," but all recent writers agree that the involvement of the lung is secondary. When the air-passages become implicated by these tumors "hair-spitting" occurs, due to the cyst opening into the air-passages. The inner wall of these cysts is, as a rule, beset with the teat-like processes so common in ovarian dermoids.

Various explanations have been offered as to the origin of mediastinal dermoids. It is known that dermoids arise in the skin covering the front of the sternum, and it seemed reasonable to attribute the mediastinal varieties to portions of skin sequestered during the fusion of the lateral halves of the sternum. This may at least account for those lying anterior to the pericardium. Other writers attribute them to imperfect closure of the lower branchial clefts, and particularly the parts concerned in the formation of the thymus gland. Some cases of great interest have been reported which show that mediastinal dermoids have a deeper meaning. Ritchie has described a dermoid which was found in the mediastinum of a man twenty-four years; attached to and forming part of its wall was a solid tumor containing tissue resembling, and indeed identical with, that of chorion-epithelioma. The lung contained many secondary nodules and there were several in the liver. This brings mediastinal dermoids into comparison with the malignant embryomata of the ovary.

Examples of typical teratomata occurring in the thorax have been recorded.

In the observations regarding parasitic fetuses attached to the external parts of the autosite it was mentioned that they rarely caused more trouble than can be described as inconvenience, but when parasitic fetuses grow within the abdomen they are grave sources of danger, and it is remarkable that in some of the cases at least the parasitic fetus or teratoma is enclosed in a cyst and resembles an ovarian embryoma. A case of great interest in relation to this subject was described in 1808 by Young, under the title "A Fetus found in the Abdomen of a Boy." In this instance a large tumor containing a good deal of fluid was found in an infant about one year old. The post-mortem examination was very carefully conducted. The cyst lay behind the peritoneum. This cyst contained the pelvis, lower limbs, and genital organs of what would be called, had it been separate from the child, an acardiac fetus.

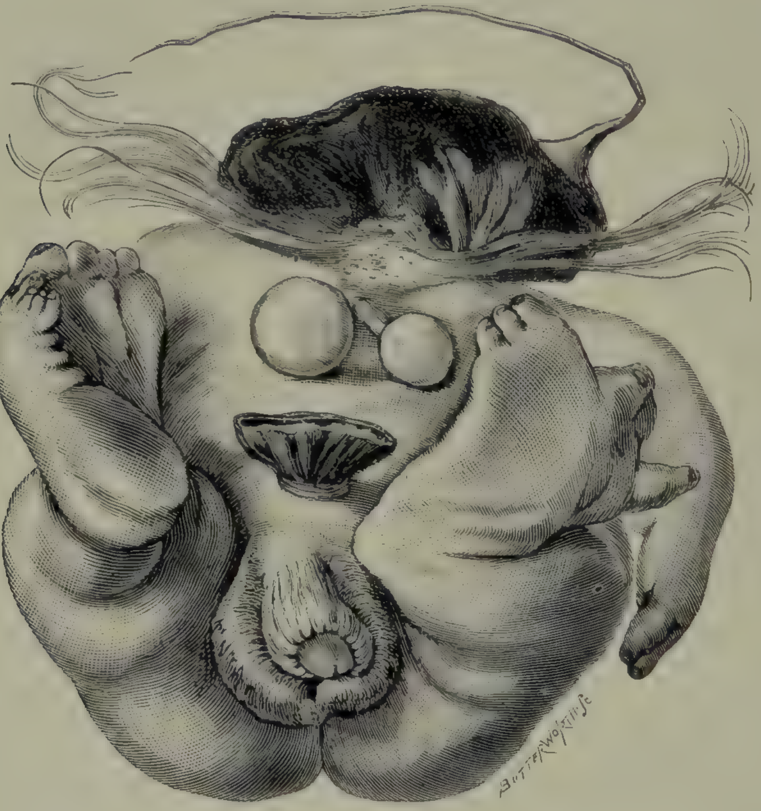

FIG. 231.—A FETUS WHICH WAS FOUND ENVELOPED IN A CYST IN THE ABDOMEN OF A BOY (Young).

Five years later Phillips in a letter to Sir Benjamin Brodie described a case in which parts of a fetus were found in a tumor situated in the abdomen of a girl two and one-half years of age. The brief description contains the statement: The cyst in the abdomen contained fluid and solid matter; the latter contained a large bone resembling a tibia covered with muscle and small bones like a tarsus. There were cystic spaces containing sanious fluid. The liver bore marks of inflammation and was studded with tubercles.

Lexer has described a fist-sized tumor removed from a girl seven weeks old; it was situated in the foramen epiploicum and lay under the liver. The tumor had cystic and solid contents. The solid portions represented skeletal and visceral elements, the whole forming a teratoid tumor.

Intracranial Teratomata.—In the section dealing with sequestration dermoids (p. 823) it was pointed out that those dermoids which are found in connection with the scalp, and in association with the tentorium, are satisfactorily explained as arising from portions of skin sequestered in the course of the development of the skull. Such dermoids display the same characters as those so commonly found near the angles of the orbits. Complex tumors of the teratoid type are occasionally found at the base of the skull, especially in association with the pituitary fossa. Teratomata in this situation resemble those which are found from time to time in the pharynx, and are composed of connective tissue, bone, striped muscle fiber, hyaline cartilage, glandular tissue, and cysts lined with squamous epithelium. In one carefully described specimen ganglion cells and white nerve fiber existed; some of the bundles had a cross-section as big as the radial nerve. I had an opportunity of studying this specimen microscopically.

Cases of this kind have been described by Lawson, Bowlby, Hale White, and Sainsbury.

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Ritchie: "Trans. Obstet. Soc. London," lv, 250.
Sainsbury: "Trans. Path. Soc. London," xxxvii, 57.
White (Hale): "Trans. Path. Soc. London," xxxvi, 37.
Young: "A Fetus found in the Abdomen of a Boy." "Medico-Chirurg. Soc.," 1808, i, 234.

It has already been pointed out in dealing with ovarian cysts that the ovary, like so many extremely specialized organs, is compound, and that the dermoids (embryomata) arise in the oöphoron or egg-bearing segment. I had been puzzled by finding an ovarian cystic tumor with an irregular layer of tissue around its walls composed of gland spaces lined with large epithelium furnished with cilia. Walthard has published the results of a careful histologic examination of the ovary, and describes the occasional presence of small cysts in this organ lined with cylindrical cells without any tendency to form warts, and in some the epithelium is columnar and ciliated. Facts of this kind tend to make us very careful in the classification of ovarian cystic tumors, for it is very hard to state with any precision the source of these small epithelium-lined cysts, but Walthard draws attention to the existence in the ovary of small epithelial bodies which have no connection with the ovarian follicles, and which he believes to arise from the cell-bundles which dip into the ovarian stroma and out of which the true ovarian follicles evolve.

In addition to these cell-bodies we must not lose sight of the fact that the hilum of every human ovary is composed of the vestiges of the mesonephros (Wolffian body), and that it is not unusual for this tissue to contain tubules with a definite epithelium. Several observers, including Alban Doran and myself, pointed out that this vestigial tissue is the source of the remarkable wart-bearing cysts which, though by no means common, are nevertheless such clinical entities as to need careful and separate consideration.

A description of these cysts is included in this section on dermoids not because they are related, but to show what a complex and vestige-containing organ the ovary is.

Papillomatous cysts of the ovary differ from the simple form of ovarian cyst in having their inner walls beset with soft dendritic warts. In their early stages these cysts do not affect the shape of the ovary until they attain an important size. The warts vary greatly in number; some cysts contain few, in others they are so luxuriant as to burst the cyst-wall and then protrude as a luxuriant cauliflower-like mass. In some cysts the warts will erode the wall at several points and grow out as soft epithelial buds. These peculiarities are sources of danger to the patient because the active surface cells are detached and engraft themselves on the peritoneum and form independent warts, and their number is often prodigious. The dispersal of germinating cells is no doubt largely assisted by the movements of the intestines, in addition to the sudden inundation of the pelvis when the cyst bursts, but there is an additional complication, which not only favors epithelial infection, but is in itself inimical to life, namely, hydroperitoneum, which is a constant sequel of the bursting of a papillomatous cyst, and the growth of warts on the peritoneum. It has been clearly established that when papillomatous cysts have been removed, there is a great probability that the peritoneal warts will disappear. This is a fact of great clinical importance, because it has happened on many occasions that surgeons have opened the abdomen to remove an ovarian cyst, and finding the peritoneum dotted with innumerable warts associated with free fluid in the belly, have abandoned the operation under the impression that the disease was malignant. The disappearance of peritoneal warts after the removal of the papillomatous cysts—for they are nearly always bilateral—is an interesting fact, and may probably be explained in this way. The life of multiple warts is often very transient, and this is probably the case with peritoneal papillomata; but as long as the seed-supply continues, new warts spring up, last for a time, and die, to be succeeded in their turn by a new crop. When the source of the epithelium cells is removed by operation, the warts then existing die and the crop is not renewed. Exceptionally papillomatous cysts rupture into the connective tissue of the mesometrium, and I have seen them clustering around the urachus as high as the umbilicus.

It is an important matter to draw a distinction between epithelial grafts, which are a feature of papillomatous cysts of the ovaries, and the carcinomatous generalization or metastasis due to the deportation of cancerous cells by lymph- and blood-vessels. It must, however, be stated that some papillomatous cysts of the ovaries exhibit distinctly malignant characters by recurring locally. Pozzi has especially emphasized the fact that a great number of patients from whom bilateral papillomatous cysts are removed make a complete and durable recovery; this I can also affirm from my own experience, but it is difficult to assert that recovery is permanent in the face of the following record: In 1878 Pozzi removed bilateral papillomatous cysts of the ovaries attended with very abundant hydroperitoneum from a woman twenty-five years of age; recovery was complete for twenty years. In 1898 the hydroperitoneum reappeared and a second operation was performed, but the recurrent tumor could not be removed; the peritoneal cavity was drained and the patient made a temporary recovery. She died a year later. Pozzi also writes favorably of the advantage of operating whenever it is possible on recurrent papillomatous masses, even when they cannot be completely removed, for such a proceeding, accompanied by temporary drainage, is distinctly advantageous to the patient.

Probably one of the most remarkable cases on record illustrating the non-malignant character of papillomatous cysts occurred in Guy's Hospital. In this instance a woman was tapped for ascites between August, 1884, and April, 1894, two hundred and ninety-nine times; on re-admission for the three hundredth tapping, she died. At the post-mortem examination a papillomatous cyst was found in connection with each ovary which could have been easily removed. The peritoneum was beset with warts.

In most cases papillomatous cysts admit of easy removal, but occasionally they burrow deeply between the layers of the mesometrium by the side of the uterus. In 1899 I removed from a woman aged forty years bilateral papillomatous cysts with many liters of free peritoneal fluid. In 1905 the patient again come under observation with a large tense cyst in the hypogastrium as big as her head. I enucleated it and found the cyst contained turbid fluid and the inner wall beset with an abundant crop of soft but not very vascular papillomata.

Papillomatous cysts are most frequent between the twenty-fifth and fiftieth years. They are the rarest variety of cyst which arise in connection with the ovary. In dealing with them from the operative standpoint it may be stated that if the disease is unilateral and the patient be near the menopause, it is a wise precaution to remove both ovaries; in younger women the healthy ovary may be left, even at the risk of a second operation. In those cases where the cysts burrow deeply in the mesometrium and there is much disturbance of the parts, it will simplify the operation and secure for the patient additional safety if the uterus be removed also, for the clinical evidence shows that these papillomatous cysts are locally malignant.

Lutein Cysts (Cystic Corpora Lutea).—Perhaps the most familiar naked-eye feature displayed on the cut surface of a mature ovary is the yellow body known as the corpus luteum. The peculiar change this body undergoes coincident with pregnancy has been the subject of much careful investigation and speculation, in connection with chorion-epithelioma (see p. 816).

Cystic corpora lutea are interesting in themselves. All who have worked seriously at the pathology of ovarian cysts have been struck by the frequency with which they are converted into cysts. Rokitansky long ago observed that corpora lutea are occasionally converted into cysts, and held the opinion that they might enlarge and form tumors of sufficient size to become clinically important, and cysts of this kind do attain a size sufficient to admit of detection in the course of a careful bimanual examination. In the course of some observations on ovarian cysts I detected that the lutein cysts of the size of a ripe cherry are easily recognized because of the thick layer of yellow material, but as the cysts increase in size the lutein tissue is spread out and becomes less and less obvious, until it fades away and leaves a transparent thin-walled cyst, which would not be regarded as a lutein cyst unless it was very carefully examined in a good light and with the definite object of searching for this particular tissue. It has been shown by Lockyer that an ovary may contain two or even a cluster of lutein cysts and the condition may be bilateral: in this event the consequent enlargement of the ovaries is such that on physical examination a tumor of some size can be detected on each side of the uterus.

Axial Rotation of Ovarian Tumors.—It is now well known, since Rokitansky drew attention to this accident in 1860, that abdominal tumors and certain of the viscera are apt to rotate and twist their pedicles, a movement which constricts the vessels supplying the tumor or viscus which has undergone torsion and gravely disturbs their nutrition and occasionally causes disaster to the individual.

That a tumor hanging freely in the belly should, by mere alteration of the position of the body, or by motion imparted to it by a tumult of the bowels, spin round and twist its pedicle is as comprehensible as the fact that a good weathercock moves in varying directions under the influence of the wind. It is, however, puzzling to find the spleen, distended Fallopian tubes, undescended testes, the pregnant uterus, the kidneys, the cecum, and the stomach liable to a similar rotation.

The phenomenon of axial rotation has been most carefully studied in connection with ovarian tumors. Concerning its probable cause many guesses have been made, such as the alternate distention and evacuation of the bladder, or passage of feces through the rectum. It is certain that sudden movements, such as a slip or a fall, or unusual exertion will cause an ovarian tumor to rotate. It has been established by a large number of carefully recorded observations that axial rotation of an ovarian tumor is common when this disease is complicated with pregnancy or is associated with a uterine fibroid large enough to fill the pelvis.

When both ovaries are converted into tumors the risk of rotation is nearly the same as when pregnancy and an ovarian cyst are associated. When both ovaries are cystic and pregnancy ensues, the risk of axial rotation is more than doubled. The torsion may occur early in pregnancy or be delayed till delivery or miscarriage. In one instance at least, in a case of bilateral ovarian dermoids, both tumors had twisted their pedicles (Doran).

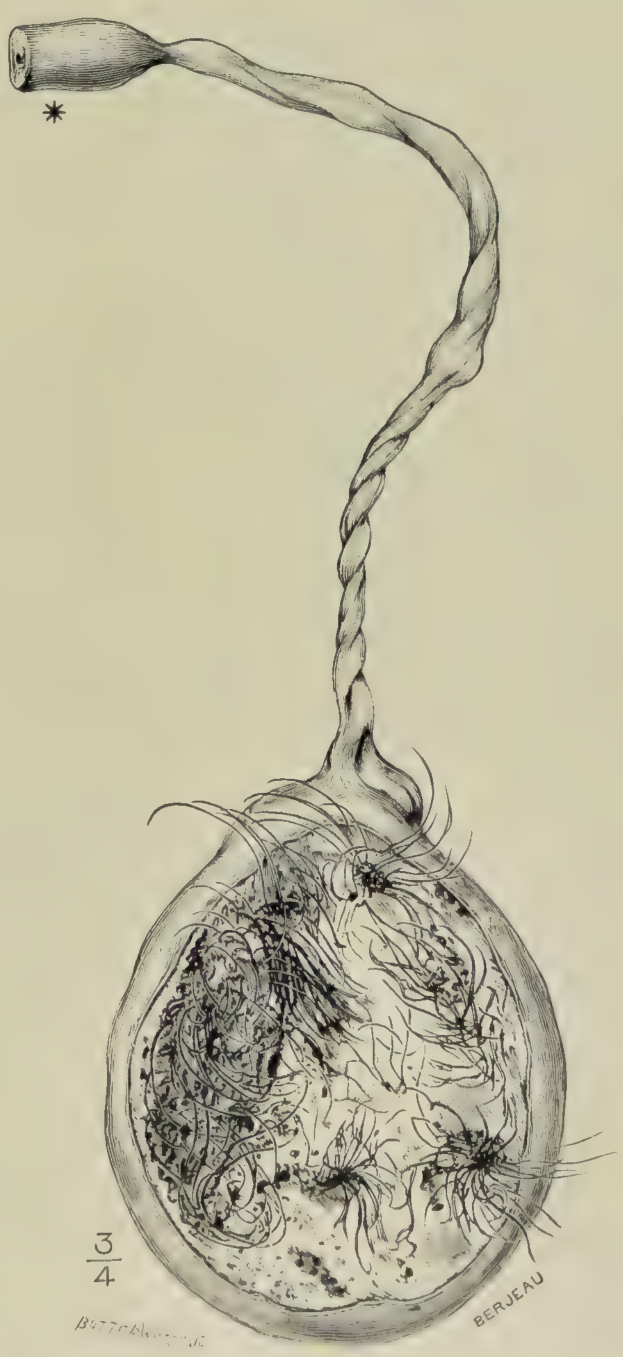

Fig. 232.—An Ovarian Dermoid Filled with Hair and Grease Which Had Twisted Its Pedicle Many Times.

The occurrence of acute torsion immediately after delivery is due to the rapid diminution in the size of the uterus and to the movement which this organ, as it sinks into the pelvis, imparts to the tumor.

Rotation of a cyst in the early stages of pregnancy is probably due to the gradual enlargement of the uterus displacing the tumor upward; and as the pressure is exerted upon one side of the cyst, it would be in a favorable position to impart a rotatory motion to a non-adherent cyst. The *amount* of rotation varies greatly. In some cases the cyst has only turned through half a circle; in others as many as twelve complete twists have been counted. The direction of the rotation may be from right to left, or *vice versâ*, but cysts exhibit a strong tendency to rotate toward the middle line rather than from it. Tumors of the right and left side are equally liable to rotate. Small tumors rotate more freely than large ones and a long and slender pedicle favors its occurrence. The force with which some of the large cysts rotate is very great, for in some instances the uterus is involved in the twist.

In one remarkable case the ovary has been caught by the pedicle and completely divided (Comyns Berkeley) (Fig. 233).

The **effect** of torsion on the circulation depends on the tightness of the twist, and this varies with the thickness of the pedicle. The vessels in a long thin pedicle would suffer obstruction more quickly than those in a short and thick one. When a pedicle is torsioned the thin-walled veins become compressed, while the more resilient arteries continue to convey blood to the cyst. The result is severe venous engorgement, and this leads to extravasation of blood into the cyst wall; in many cases the veins rupture, and hemorrhage takes place into the cavity of the cyst. The hemorrhage may be so profuse as to cause profound anemia, and even death.

When the venous circulation is completely arrested in consequence of torsion, the appearance of the cyst is very striking and characteristic. On opening the abdomen during life, instead of the cyst presenting the familiar white glistening appearance, it has a deep, dark, lusterless hue, which is most intense near its attachment to the pedicle. In milder degrees of torsion the change in color only affects the base of the tumor. The pedicle on the distal side of the twist presents the same dark hue, but on the uterine side it is of natural tint. The contrast of color in the two parts of the pedicle is very striking. The walls of the cyst are thick and succulent; the blood contained in the cavity, or in the loculi if multilocular, may be of a chocolate color.

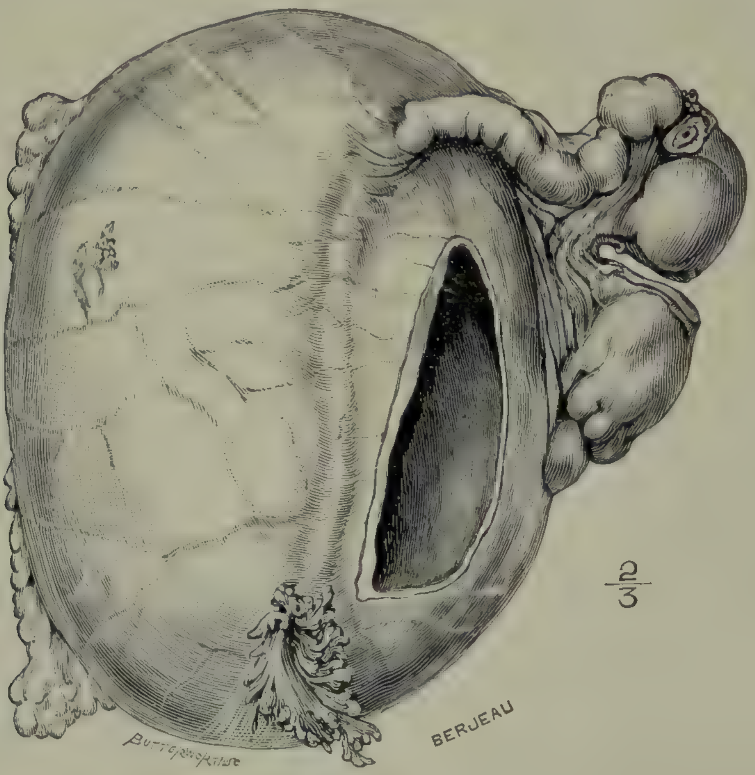

FIG. 233.—A PAROVARIAN CYST WHICH HAD ROTATED AND TWISTED ITS PEDICLE. The ovary was caught in the pedicle and divided in halves (Comyns Berkeley).

When such a cyst is removed from the body and the blood allowed to drain away, or is washed away by a gentle stream of water, the tissues will resume their natural color. This should be remembered, because some writers have attributed this dark color to gangrene of the cyst. This is erroneous; gangrene of an ovarian cyst is a rare event, and can take place only when air is admitted from without, as during the operation of tapping, or when intestinal gases or fluids obtain access to it.

The usual effects of acute torsion of the pedicle are passive congestion, thrombosis, extravasation of blood into the tissue of the tumor, and necrosis.

Necrosis is localized death, in contrast to death of the organism as a whole, or "somatic death."

Moist gangrene is necrosis followed by decomposition and putrefaction of the dead tissues. When soft parts necrose in situations where they are accessible to putrefactive organisms, such as the exterior of the body, the lungs, or the intestinal tract, decomposition rapidly ensues, especially if the parts contain much blood. In the case of ovarian tumors with twisted pedicles, not in communication with the outer air directly or indirectly, microörganisms can rarely gain access to them and cause decomposition. It is therefore erroneous to describe as gangrene the changes observed in cysts with torsioned pedicles. This is further illustrated by the circumstance that small ovarian tumors may be completely twisted from their pedicles and subsequently shrink. If the changes in the cysts were gangrenous, general infection of the peritoneum and death would be the inevitable consequences.

Rotation of an ovarian cyst when it gives rise to such severe changes as have just been considered may be described as *acute torsion.* It frequently happens that during the performance of ovariotomy a thick pedicle is found twisted through half or even a complete circle, without producing an appreciable effect upon the tumor. In others, torsion takes place so gradually, yet so completely, that the pedicle is twisted like a rope, and not infrequently the pedicle breaks and the tumor becomes detached from its uterine connections. To this variety the term *slow* or *chronic torsion* may be applied. Its effects are not less interesting than those which follow acute twisting. When rotation occurs slowly, the walls of the cyst inflame and adhesions are established between the cyst and the omentum or the parietal peritoneum; such adhesions become vascular and maintain the vitality of the cyst wall after the circulation through the pedicle is arrested. Cysts have been observed in all stages of transplantation.

Acute torsion is more frequent in tumors of medium size; it also occurs in small cysts; but it is the small tumors, especially dermoids, in which slow torsion takes place.

The dermoid which had undergone axial rotation (Fig. 232) had so lengthened its pedicle that the tumor sometimes rested on the loin and resembled a very movable kidney; it produced no pain, but annoyed the patient by its excursions about the belly.

The symptoms of acute torsion of an ovarian cyst are often so characteristic as to lead to a correct diagnosis. When a woman complains of sudden and violent pain in the abdomen, accompanied with vomiting, and she is known to have an ovarian tumor, or she presents herself for the first time to the surgeon, and these signs are associated with an abdominal swelling the physical signs of which are indicative of an ovarian tumor, axial rotation should be suspected. Should the patient possess a gravid uterus as well as an ovarian cyst, it is even more probable that rotation has occurred; or if she has an ovarian tumor and has been recently delivered. this is an additional reason for suspecting that the symptoms arise from a twisted pedicle.

Clinical observations demonstrate that the predominant signs of acute axial rotation of abdominal tumors and viscera are those common to a strangulated hernia minus stercoraceous vomiting.

Even the presence of fecal vomiting does not always negative the existence of acute axial rotation of an ovarian tumor, for a loop of bowel may be involved in the twist and produce intestinal obstruction.

Otto von Franque has observed in a new-born child an ovarian cyst, the size of a dove's egg, with a tightly twisted pedicle.

Suppuration in Ovarian Dermoids.—When air or intestinal fluids gain access to these tumors, then septic infection with all its attendant evils is the result, and unless the pus finds an outlet the patient dies. The pus in a suppurating dermoid sometimes bursts into the bowel, bladder, vagina, or through the abdominal wall at or near the umbilicus. When the cyst communicates with the bladder it will sometimes entail very great misery, because fragments of bone, teeth, locks of hair, and sloughs become impacted in the urethra. Cystitis is an almost constant accompaniment. Ovarian teeth in the bladder have formed the nuclei of phosphatic calculi.

Hair from ovarian dermoids entering the bladder is voided with the urine, a condition of things described by French surgeons as *pilimiction.*

Rupture.—Ovarian cysts of all kinds are liable to burst into the belly either without any obvious cause (spontaneous rupture) or from violence, for example, during an immoderate fit of laughter, vomiting, coughing, falls or blows upon the belly, etc. Some of the effects of the bursting of an ovarian cyst have been already considered.

Mode of Death.—Tumors of the ovaries are now so promptly removed when discovered that there are happily few opportunities of studying the ways in which they destroy life. The chief modes are the following: (1) Pressure on the ureters, leading to hydronephrosis and uremia; (2) cystitis and pyelitis; (3) intestinal obstruction; (4) suppuration of the cyst and septic infection from leakage (peritonitis); (5) hemorrhage from rupture of the cyst; (6) axial rotation of the tumor; (7) impediment to delivery; (8) epithelial infection of the peritoneum and occasionally dissemination (malignancy).

Treatment.—*All ovarian cysts and tumors should be removed entire at the earliest possible moment.*

Dermoids (Embryomata) and Chondrifying Tumors of the Testis.—It is a matter of prime importance to distinguish between dermoids of the scrotum and those intimately associated with the testis. Scrotal dermoids belong to the sequestration group and lie outside the tunica vaginalis; true testicular dermoids are of different origin.

Few surgical writers appreciate the extreme rarity of testicular dermoids. During the last half century, as far as I can ascertain, scarcely twenty cases have been recorded in Continental surgical literature. During the last twenty-five years two cases have been published in England, and of these one came from India. A third example, which will now be described, I owe to Dr. Booth, of Hankow, Central China. The following is his account of the clinical facts:

A blind boy, sixteen years old, with an enlarged testis, has been in our blind school (Hankow) for nine years. The boy says his mother told him "he had it when he was born." He had frequent inflammatory attacks of the scrotum following injury, such as crushing against a stool, etc. He came to the out-patient clinic during one of the attacks, which rapidly subsided under an evaporating lotion.

At the operation the right testicle was small, but normal in position. The skin over the front of the left testicle was reddened, and a sinus existed at the junction of the scrotum and penis; the testicle appeared as a globular, tense, but elastic mass, as though filled with fluid, and no distinction could be made between the body of the testis and the epididymis. The spermatic cord was thickened.

In the course of the operation some pus escaped from beneath the reddened skin; otherwise the organ was shelled out and removed entire without any difficulty. The sinus and the adherent skin associated with it were exsected, and the edges of the skin brought together with sutures and the wound drained. The boy made an uninterrupted recovery.

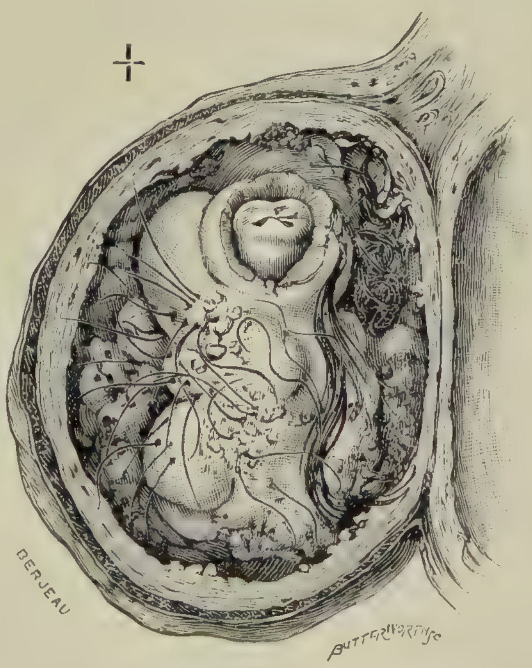

Fig. 234.—A Dermoid of the Testis Shown in Section (Museum Royal College of Surgeons, London).

The tumor (Fig. 234) is globular, with a diameter of 5 cm.; near the lower pole it presents an irregular body. The walls of the tumor are thick and gristly, resembling thickened tunica albuginea, but the whole mass was invested by a delicate tunica vaginalis. The cavity of the dermoid contained the usual sebaceous matter mixed with loose hairs, and a sessile body of irregular shape consisting of bone and hyaline cartilages covered with tissue, which to the naked eye looked like mucous membrane. Embedded in the upper end of this tissue there was a multicuspidate tooth resembling those found in ovarian dermoids, its crown still covered with mucous membrane. The soft investing tissue also possessed some delicate lanugo-like hairs. Microscopically the tissue was found to be covered mainly with stratified epithelium; in some parts it exhibited a single layer of columnar and subcolumnar cells. Sebaceous glands were fairly numerous.

A very careful but unsuccessful search was made for the vas deferens, and I failed to find any evidence of testicular tissue, but Mr. S. G. Shattock carefully re-examined the wall of the tumor and succeeded in demonstrating the presence of a thin layer of well-developed testicular tubuli lying beyond the dense fibrous tissue composing the chief thickness of the cyst wall. On the opposite side of the specimen to that shown in the drawing he also succeeded in finding the epididymis. The importance of this observation is very great in regard to the relation of the dermoid to the testis proper.

In its gross anatomy and structural details this tumor reveals the usual features of dermoids growing in relation with the testis. Some, it is true, are more complex and contain nerve cells, as in one very carefully reported case examined by Cornil—in a "bud" growing from the cyst-wall a collection of nerve-tissue containing ganglion cells was detected.

In its clinical details the tumor did not differ from its forerunners. There is a remarkable uniformity in this respect. In nearly all the recorded cases enlargement of the testis was observed at or shortly after birth. In a fair proportion the patients were deprived of the affected organ in early childhood. In those who were not operated upon during infancy, the tumor seems to have caused little inconvenience; indeed, it appears to lie dormant till puberty, then bruises and knocks, or abscesses and sinuses cause trouble and lead to surgical interference.

Most of our knowledge of testicular dermoids dates from an elaborate article published by Verneuil in 1855, founded on the reports of nine cases he collected from the literature of the preceding one hundred and fifty years, and one example which came under his own observation. The conclusions expressed in this admirable paper have become classic, and form the foundation of our knowledge of the subject; and even at this date, nearly half a century since its publication, Verneuil's views are reproduced (frequently without any reference to, and often, perhaps, in ignorance of, their source) in monographs devoted to diseases of the male genital organs and in text-books of surgery. It is true, notwithstanding the fact that these tumors can now be studied with all the advantages of modern histologic methods and differential staining, that we know no more concerning their pathogenesis than Verneuil, and testicular dermoids remain with us, as with him, pathologic curiosities.

It is also noteworthy that dermoids of the testis, according to all the available records, are unilateral, whereas ovarian dermoids are very frequently bilateral.

Verneuil shows in the title of his paper ("Mémoire sur l'inclusion Scrotale et Testiculaire")—which title, he relates, was selected as conveying precisely the view he held in regard to the nature of the disease—that he believed that testicular dermoids belonged to the class of double monsters known as parasitic fetuses. A study of the records published during the last ten years supports Verneuil's contention that dermoids within the tunica vaginalis, though attached to and often intimately associated with the testis, are not really "of the testis" in its strictest sense; they do not arise from transformation of testicular tissue, but whether they should be regarded as parasitic fetuses (teratomata) is another question, and one which requires further consideration and elucidation. In some of the cases the dermoid was attached to the gland by such slender connections that the surgeon succeeded in detaching the tumor and preserved the testis. Admirable conservative operations of this character are recorded by Cornil and Berger, Chevassu and Réclus.

Horses are especially liable to dermoids, a fact known to Verneuil; and they are often associated with undescended testes. Like typical ovarian dermoids, they contained an ill-developed embryonic rudiment contained in a cyst, covered with pilose skin and stuffed with loose hair, grease, and occasionally teeth resembling equine incisors.

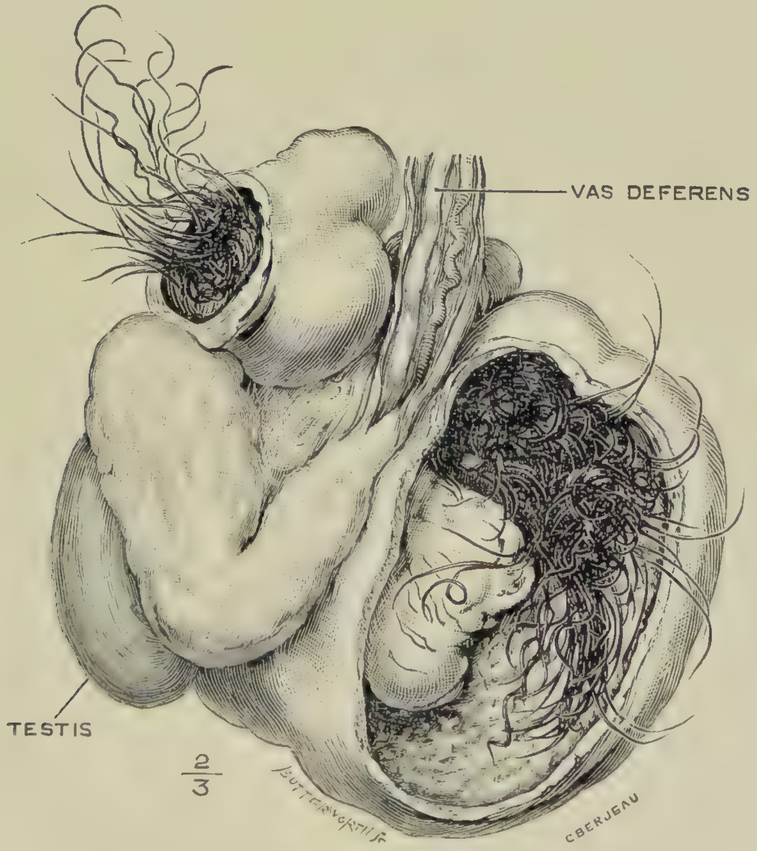

FIG. 235.—UNDESCENDED TESTIS REMOVED FROM A COLT.
It is associated with a large dermoid containing grease and coarse hair like that of the mane and tail.

The hair resembles that of the mane or tail. In all the specimens I have seen the dermoid, though attached to the testis and the epididymis, lay outside the tunica vaginalis, a fact mentioned by all writers on this matter.

The occurrence of dermoids in the undescended testes of horses has a clinical interest, for, as I have already mentioned in the records of the human cases, although the unusual size of the testis was invariably noticed at birth, yet it did not interfere with the descent of the organ. There is a case recorded by Delbet in which a testis, retained at birth in the inguinal ring, gradually descended to the scrotum; subsequently it was found to be occupied by a dermoid. In this respect horses and boys differ very markedly, but they agree in the following points: that though a dermoid may be attached to, or incorporated with, either a right or a left testis in fairly equal proportions, an example of bilateral testicular dermoid has yet to be recorded. In this respect the testes are in marked contrast with ovaries, for ovarian dermoids are very frequently bilateral.

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It is an interesting feature of the writings concerning dermoids of the testis that the majority of the observations, and certainly the best among them, have been the work of French surgical writers. It would seem that the classic monograph of Verneuil gave the subject a French domicile. The subjoined list makes no pretence to completeness, but furnishes references to the best known and most easily accessible records, in which the details are related with sufficient care and completeness to make them useful either for the surgeon or the pathologist:

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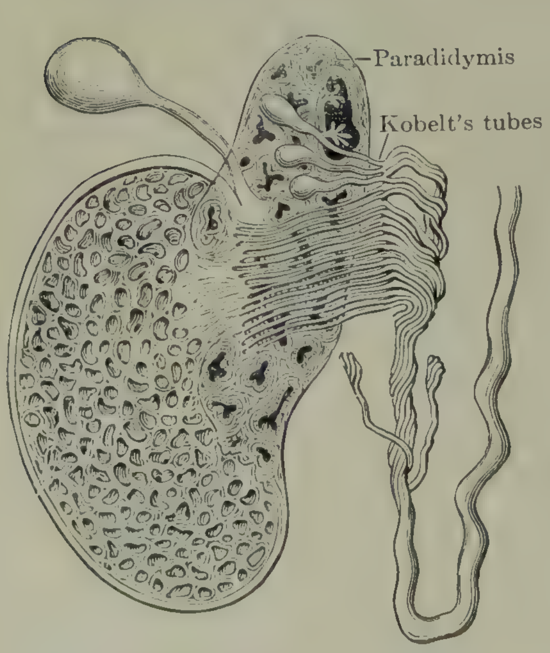

FIG. 236.—DIAGRAM TO SHOW THE RELATION OF THE MESONEPHROS AND ITS DUCTS TO THE ADULT TESTICLE (from Bland-Sutton "On Tumors").

Chondrifying Tumors of the Testis.—More than fifty years ago it was recognized that malignant tumors of the testis are liable to contain hyalin cartilage, and among the earliest examples of this is the classic case described by Paget in 1855. The specimen is still preserved in the museum of St. Bartholomew's Hospital. In this instance a man thirty-seven years of age had his right testicle removed on account of a tumor involving both the testicle and the spermatic cord. Some weeks later signs of pulmonary disease appeared and the man quickly died. At the autopsy the lungs presented numerous secondary nodules of hyalin cartilage. A mass of secondary growth adhered to the vena cava near the termination of the renal veins, and a process of the growth had perforated the wall of the vein and projected into its lumen.

A very large amount of patient investigation has been devoted to the histology of malignant tumors of the testis, partly to determine the nature of the chrondrification of the tissues, and partly to determine the testicular tissues in which they arise. It is also a fact that nearly all writers on malignant tumors of the testis are unanimous in classifying them among sarcomata, notwithstanding that, contrary to what is usual among sarcomata as a genus, infection of the abdominal lymph glands is the invariable rule.

As long ago as 1853, Curling published a careful account of tumors of the testis, and especially of the form known as "general cystic disease" of this organ, and drew special attention to the presence of hyalin cartilage in these tumors; he also pointed out that the tumors arise in that part of the gland known as the rete testis, and his views on this subject have been amply confirmed by subsequent writers. Between the globus major of the epididymis and the testis exist remnants of the mesonephros known as the paradidymis, and this structure is continuous with the connective tissue forming the hilum of the testis, and it is traversed by the efferent ducts of the testis. The majority of the malignant as well as the benign tumors of the testis arise in this situation, and as such a tumor increases in size it compresses and ultimately flattens out the true secreting tissue of the gland. If examples which do not exceed the size of an egg be bisected, the secreting tissue will be found flattened out like a strap. In large specimens it is often difficult to detect any remnant of the testicular tissue. In children it is often necessary to determine this question with the aid of a microscope.

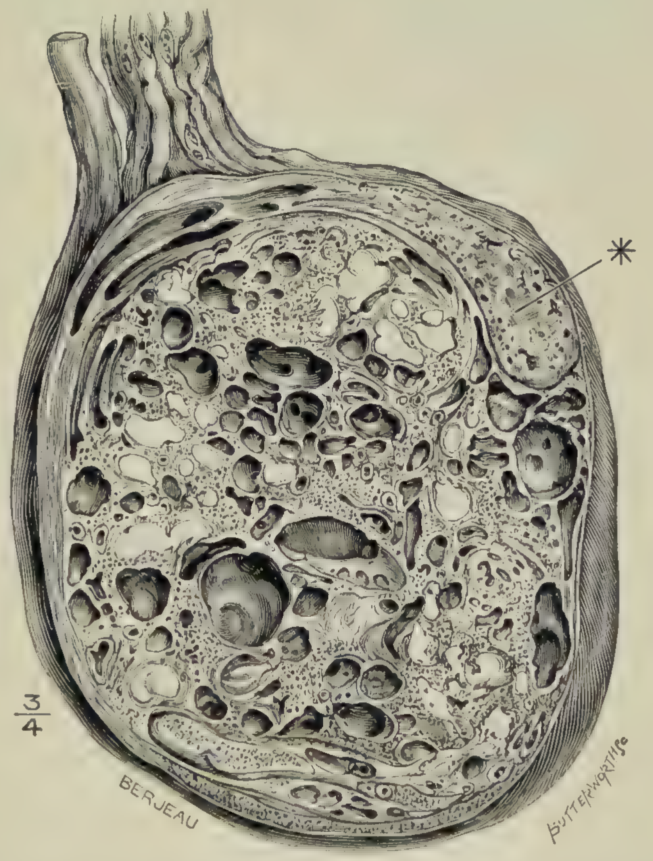

FIG. 237.—SO-CALLED GENERAL CYSTIC DISEASE OF THE TESTIS.

*. The compressed testis (Museum Royal College of Surgeons).

When we come to consider the names applied to tumors of the testis we find the subject obscured by a fog of names. Some are described as cystic sarcomata, cystic fibromata, myxomata, and the like, all unfortunate names. The best known are those included in Curling's term "general cystic disease of the testis," of which he recognized an innocent and a malignant form.

These tumors in their typical condition are made up of large numbers of cystic spaces, which vary greatly in size; some are no larger than rapeseed, others may attain the size of a hazelnut. Many are distinctly tubular, and the cysts may communicate with each other. The loculi are lined with regular columnar, cubical, or stratified epithelium, and intracystic papillomata are not uncommon. The connective-tissue framework of the tumor consists mainly of simple fibrous tissue, but it may be so abundant as to form the bulk of the tumor, the cysts being sparse. In some of the specimens, especially those met with in infants, plain muscle fiber has been detected.

It is reasonable to believe with Eve that the tubules and cysts found in these tumors originate in the tubules and vasa efferentia of the testis, and it is impossible to deny that some of them arise in the glandular structures of the paradidymis.

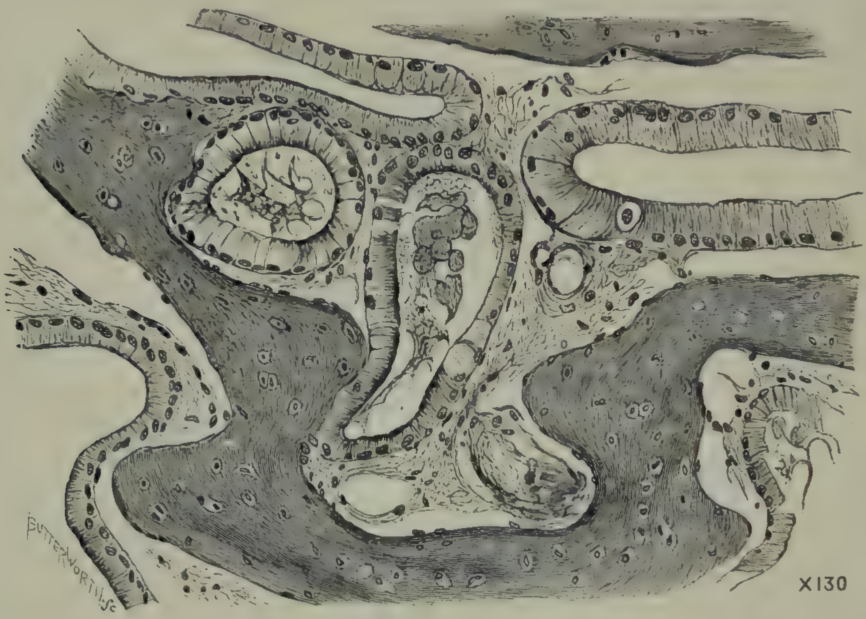

FIG. 238.—TYPICAL HYALIN CARTILAGE IN THE STROMA OF A RECURRENT CARCINOMA OF THE SPERMATIC CORD (after Foulerton).

In nearly all writings on the subject of malign tumors of the testis it is customary to class them as sarcomata, in spite of the undeniable existence of epithelium. Foulerton has recently shown that many malignant tumors of the testis are in structure and in pathologic tendency carcinomata, and he is of opinion that writers on surgical pathology are in the habit of considering the presence of hyalin cartilage as evidence that the tumor is a sarcoma, and the presence of this tissue in typical cancers has not been sufficiently considered. He has, however, proved in an unequivocal way that hyalin cartilage occurs in association with cancer of the rectum and has proved its presence in a lymph gland infected with carcinoma.

Foulerton is also of opinion that many if not the majority of malign tumors of the testis are more properly classed with the carcinomata than with the sarcomata, and he points out that Paget's classic specimen when re-examined by Kanthack and Pigg was found to be a carcinoma. At the same time he is in agreement with preceding observers that malignant tumors of the testis arise in the hilum of this organ.

No doubt much of the difficulty associated with these tumors is due to their relative rarity, for even in a large general hospital in London two cases a year is a fair average. It is also necessary to draw attention to the statement, so repeatedly found in the clinical reports of malignant tumors, that the patient attributes the onset of his disease to an accident, such as a crush or a blow.

As an example of the taxonomic difficulty experienced by systematic writers in dealing with the group to which the hilum-tumors of the testis belong, it may be mentioned that Wilms and those who follow him classify the tumors of the testis, kidney, and the salivary gland, which contain so many diverse forms of mature tissue, as "mixed tumors." It is also worthy of note that the cartilage-containing tumors of the testis are classed with the typical dermoids of that organ. If this view can be sustained, it will simplify classification and the work of the teacher very greatly.

Among the most important observations which show the complex characters of testicular tumors are those made by Schlagenhaufer. A man aged forty-three years had a tumor of his testis enclosed in a firm white connective-tissue capsule; the tumor consisted of a brown-red crumbly tissue which on microscopic examination resembled that of a typical chorion-epithelioma. The man died with secondary deposits in the left lung, thyroid gland, and right kidney. These deposits also exhibited the structure of chorion-epithelioma.

Some similar observations have been made by other pathologists, and they all agree that the naked-eye and microscopic character of the tissue is identical with chorion-epithelioma.

One of the most prominent clinical features of malignant tumors of the testis is the rapidity and extent of the lymph gland infection. The great size which the posterior lymph glands of the abdomen attain in some patients is truly astonishing. The connective tissue in the hilum of the testis is described as consisting "of fine fasciculi and laminæ of areolar tissue, these being covered and partly composed of flattened epithelioid cells. Between the laminæ and fasciculi are large cleft-like spaces, containing lymph, and almost everywhere enclosing the basement membrane of the tubules. If these spaces are injected by the puncture method, the injecting fluid flows away by the lymphatics of the spermatic cord." (Quain.) This free lymphatic communication of the hilum-territory explains the extreme facility with which the abdominal lymph system can be infected.

Dissemination of testicular sarcoma is sometimes brought about by blood-vessels, for it occasionally happens that secondary nodules are found in the skin, lungs, and other viscera. Nevertheless, the prevailing mode of infection is by the lymphatics, and this may involve the lymph glands which extend from the fifth lumbar vertebra to the root of the neck. A very careful study of the lymphatics of the testis has been published by Most.

Treatment.—A study of the effects of operation for the cure of sarcoma of the testis is very instructive, as it exhibits malignant disease in some of its worst aspects. Castration, save in very exceptional cases, is one of the safest operations in surgery. In the early stages of sarcoma the diseased testis can be completely removed. Recurrence in the wound or stump is an unusual event; but dissemination, due to infection of the aortic lymph glands, destroys more than half the patients within a year of the operation. In some of the cases the infected lymph glands parallel with the aorta form very large masses. The lymphatics from the testis run with the spermatic cord through the inguinal canal and join the lumbar lymph glands near the lower pole of the kidney. These glands are in close relation with the inferior vena cava on the right, and with the abdominal aorta on the left side; it is this intimate association with big blood-vessels which is the chief obstacle to the surgical removal of the cancerous lymph glands.

The classificatory difficulty in dealing with tumors of the testis is very great and may be briefly summarized in this way: Some writers distribute the tumors according to the preponderance of a particular tissue, and name them fibromata, myxomata, myomata, sarcomata, dermoids, etc.; others claim that many of them are truly carcinomata. Perplexed by the multiplicity of the elements which go to the making of these tumors, some pathologists prefer to call them "mixed tumors." Whatever view the pathologist takes of them, the surgeon never forgets the grim reality that the majority of these compound tumors of the testis quickly destroy the life of the individual.

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Malignant Tumors of the Kidney in Infancy (So-called Renal Sarcomata).—Some years ago no two groups of tumors seemed more widely separated or marked by such distinctive features as sarcomata, dermoids, and teratomata. These distinctions were by no means confined to their structure, but extended to the clinical or practical aspect of the question. Many careful observations have been made on the histology of tumors belonging to the testis and ovary, which have shown that many tumors of the ovary which had formerly been regarded as belonging to the so-called innocent group and closely allied to dermoids occasionally exhibit unmistakable malignancy and destroy life by dissemination. Midway between the most typical forms of sarcomata, of which those arising in connection with the periosteum of bone may be chosen as examples, and the hair and tooth-containing dermoid of the ovary, there stands the remarkable and deadly group of tumors which grow in the kidneys of infants. The great feature which distinguishes these renal tumors from dermoids is the absence of the common dermal elements, skin, hair, and teeth; but they possess glandular structures and a tissue identical with striated muscle fiber. This last-mentioned tissue is rare in ovarian dermoids and embryomata. Dermoids of the testis, however, bridge the gap between these two groups, for tumors arise in the hilum of the testis consisting of almost pure muscle fiber; others contain epithelial structures resembling the epithelial tubules of "renal sarcomata," and lastly dermoid structures as perfect and as harmless as any ovarian dermoid. The testicular tumors intermediate between the muscle-containing tumors and the dermoids, namely, those rich in ill-formed connective-tissue and epithelial tubules are as malignant as the renal tumors of infancy.

The one great embryonic event, so to speak, which brings tumors of the ovarian hilum (paroöphoron), those which arise in the rete testis (paradidymis), and renal tumors of infants which grow from the connective tissue in the renal sinus into a common group is that extraordinary temporary embryonic organ, the mesonephros (Wolffian body).

During the first five years of life the kidneys are exceptionally liable to tumors possessing peculiar characters; they originate in the connective tissue of the renal sinus, and gradually distend the cortex until the tumor is surrounded by a thin capsule formed of expanded secreting tissue of the kidney. On this account these tumors are described as being encapsuled, but it is a spurious encapsulation, formed partly by renal tissue and in part by the true capsule of the kidney. On section, such sarcomata are yellowish-white, and the cut surface is often dotted with groups of small cavities, due to secondary changes, especially when the tumor is very large.

The basis of these tumors is connective tissue containing cells of various shape and size; some are round or oat-shaped, and others are spindles. In a fair proportion of specimens many of the spindle cells present the cross-striation so characteristic of the fibers of voluntary muscle, and they lack a sarcolemma. When these cells are present, the tumor is sometimes termed a myosarcoma.

In other examples the ground substance contains groups of tubules lined with regularly arranged cubical epithelium, and in section resembling a number of renal tubules cut transversely.

A careful microscopic study of these tumors, as well as a critical analysis of the descriptions published by others, indicates that when the striped cells are very abundant the tubules are, as a rule, absent. In examples containing many tubules, as well as those in which striped spindles are numerous, the round, oat-shaped, and spindle sarcoma cells are equally abundant. A study of the fetal kidney demonstrates very clearly that the renal sarcomata of infancy arises in the connective tissue of the renal sinus. The epithelial cylinders may be due to the entanglement of uriniferous tubules, in consequence of the sarcoma invading the cortex, while the striated spindles may be derived from the muscle-tissue of the renal pelvis, which is an expansion of the hollow muscle known as the ureter.

It is a characteristic feature of these tumors that the ureter is rarely obstructed, although they attain enormous dimensions; this also explains the rarity of hematuria in the infants who possess them.

Another remarkable clinical feature presented by these renal tumors is their painlessness. A child with a very large renal sarcoma has been absolutely free from pain and amusing himself with his playmates in the garden three days before he died. Indeed, many mothers, when the gravity of a renal tumor of this kind is explained to them, will express their astonishment that a child, apparently in excellent health and spirits, could be in such serious straits as the surgeon would have them believe.

Though the ureter so constantly escapes invasion, yet the veins are always implicated; and this constitutes one of the most peculiar as well as most dangerous features of renal sarcomata in children. The tumor tissue extends into the renal vein, and often projects and even runs for a long distance into the inferior vena cava; portions are detached and carried to the pulmonary circulation, and are arrested in the capillaries of the lung, and originate secondary deposits. The intravenous apex of such an outrunner is usually cone-shaped and smooth. Occasionally a large fragment is detached, and this has been known to block the right auriculo-ventricular orifice (Osler). Such a gross embolus is uncommon. Plugging of the vena cava by an outrunner is by no means rare, and gives rise to edema of the lower limbs. In a case under my own care the inferior vena cava was completely obstructed from its origin to its termination by a sarcomatous extension of this kind.

It is a singular and well-established fact that when certain paired viscera, such as the kidneys, ovaries, eyeballs, and crura cerebri, are in early life attacked by sarcomata, in a very large proportion of cases, perhaps half the number, the disease is bilateral. In relation to this matter, Abbe recorded a very important observation. He successfully extirpated a kidney for sarcoma in a child of one year and two months. Four and a half years later the little patient again came under his care with a sarcoma in the remaining kidney. The analysis of a large number of reports shows that nephrectomy for renal sarcomata in children under six years of age has a mortality of over 50 per cent. Of the 50 per cent. that recover, forty-five die from recurrence at periods varying from two months to a year. In the remaining five life may be prolonged many years, and in a case reported by Malcolm it is known that the patient was alive and well ten years after the operation, which was performed when the patient was twenty months old.

VI.—CYSTS.

Cysts result from the abnormal dilatation of preëxisting tubules or cavities. In the simplest form a cyst possesses a wall composed of fibrous tissue occasionally mixed with plain muscle fibers and lined with epithelium; the cyst-contents may be mucus, bile, saliva, urine, etc., according to the nature of the organ in which the cyst arises. Cysts may be arranged in three groups: (1) Retention cysts; (2) tubulo-cysts; and (3) hydroceles. There are abnormal formations often classified with cysts which are better arranged as a sub-group under the title "pseudo-cysts," which embrace diverticula, bursæ, ganglions, and the complex conditions known as neural cysts, comprising meningoceles and the compound cyst-like swellings associated with the congenital defects of the vertebral column and spinal cord known as spina bifida.

In this article only tubulo-cysts will be described, for the conditions known as retention cysts will be considered in the descriptions of the organs with which they are connected, such as the gall-bladder, kidney, lacrymal ducts, pancreas, or salivary glands. The cysts known as hydroceles will be described in the chapter devoted to the "Diseases of the Male Reproductive Organs."

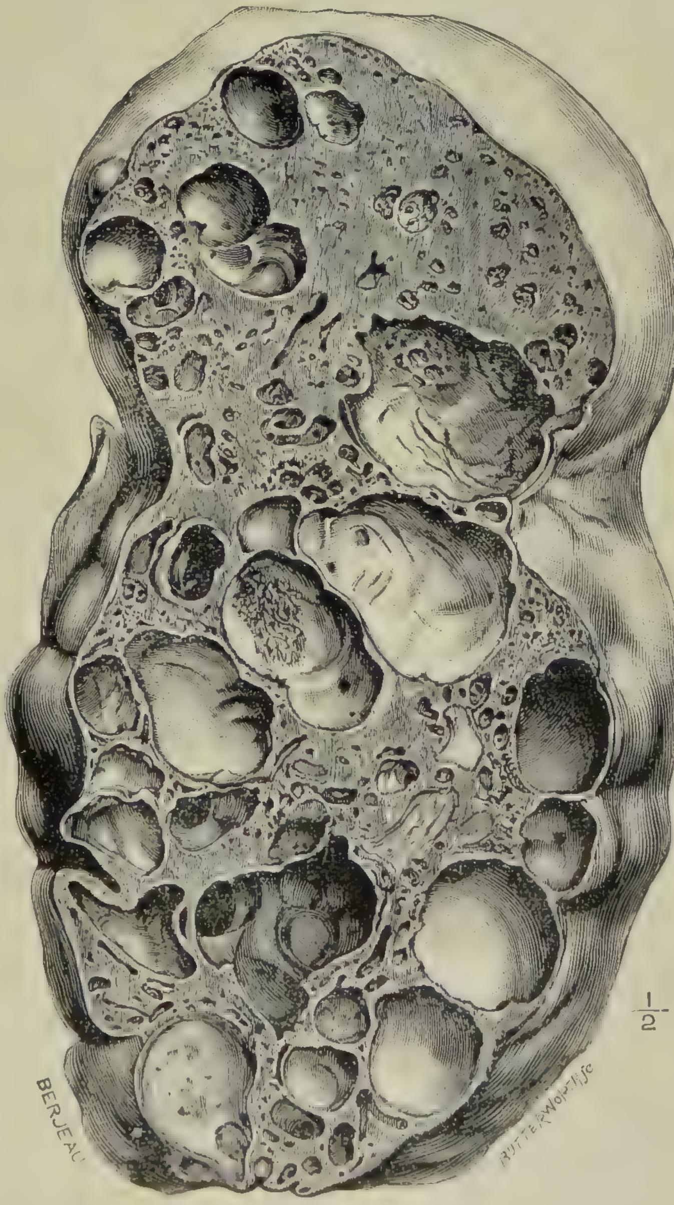

Fig. 239.—A Liver in Section to Show the Honeycomb Condition Known as General Cystic Disease.

It will be useful to illustrate the way in which cysts arise in organs permeated by narrow canals by reference to two rare forms of cysts met with in the liver. This organ is thoroughly traversed by narrow epithelium-lined passages known as bile canals, too small to be visible to the naked eye; but from causes unknown these canals dilate irregularly throughout the liver and cause it to become enormously enlarged. When the liver is divided these dilated canals cause the cut surface to appear like a honeycomb (Fig. 239). This condition is known as general cystic disease of the liver.

A remarkable feature connected with it, is its not infrequent association with a similar affection of the kidney due to pilatation of the minute uriniferous tubules. This is an insidious disease of the liver and gives rise to no diagnostic features except progressive enlargement of the organ, and it may attain a huge size. The distinguishing feature of this form of cystic disease of the liver is the fact that each dilatation remains isolated or discrete.

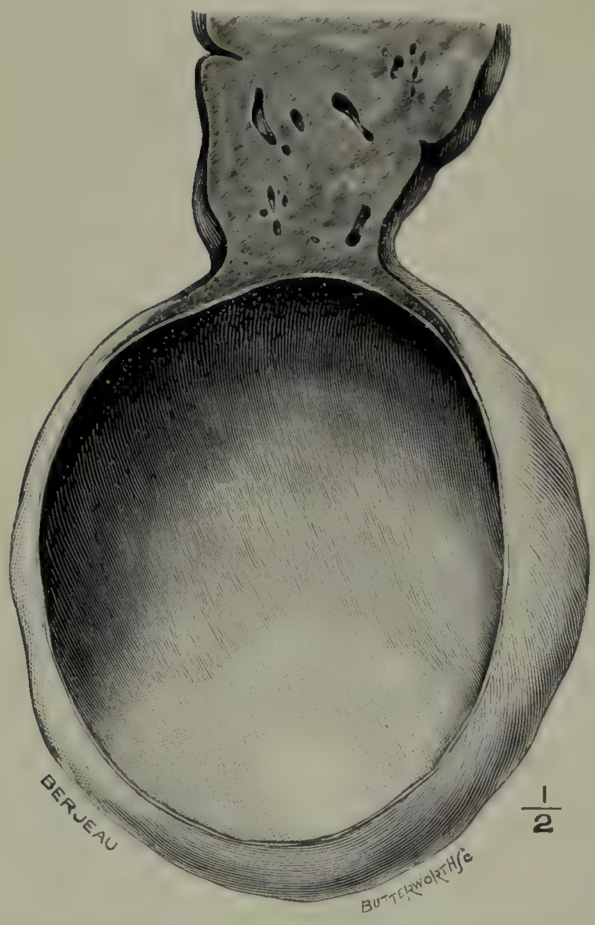

Fig. 240.—A Solitary (Non-parasitic) Cyst Growing from the Free Border of the Liver (Museum Royal College of Surgeons).

Solitary (*Non-parasitic*) *Cyst of the Liver.*—This kind of cyst is most common in adults, and at present all the examples have occurred in women. The cyst arises in the free anterior border of the liver and may attain a capacity of two pints. The walls are very thin and lined with epithelium, the outer wall being covered by a capsule directly continuous with the serous investment of the liver. The walls of the cyst near the liver show dilated bile-canals lined by cubical epithelium. The microscopic anatomy of such cysts shows clearly that they arise from the dilation of bile-canals which subsequently fuse to form a large cyst. The contents of such cysts may be bile, blood, or straw-colored fluid with negative characters (Fig. 240).

Rare as these solitary cysts are, they need consideration, for in an example which I removed from a patient aged seventy-three years, it had attained the dimensions of the woman's head and had been mistaken for an ovarian cyst by a physician; its clinical characters most strongly resembled a cyst or tumor of the mesentery.

Tubulo-cysts.—The human body, in common with that of many other mammals, contains a certain number of tubes which, so far as is known, serve no useful purpose in the adult, and may be called in consequence *functionless ducts.* Some of these—*e. g.*, the vitello-intestinal duct and the urachus—were probably useful to the embryo; others, like the parovarium and Gärtner's duct, are serviceable in the male, as they act as conduits to the testis. Functionless ducts must not be confounded with *obsolete canals;* these serve no useful purpose in man, but were, in all probability, functional in the ancestors of existing vertebrata. Both sets of canals are of interest to the pathologist, as they are the source of cysts which are not only inconvenient to the individual but actually dangerous to life. (Cystic conditions arising in connection with obsolete canals are described in the chapter on the neck.)

The genus *tubulo-cysts* includes the seven following species: (1) Cysts of the vitello-intestinal duct; (2) cysts of the urachus; (3) paroöphoronic cysts; (4) parovarian cysts; (5) cystic disease of the testis; (6) cysts of Gärtner's duct; and (7) cysts of Müller's duct.

Cysts of the Vitello-intestinal Duct.—It is not uncommon to find connected with the umbilicus of babes and young children small tumors varying in size from a pea to a cherry. These tumors are bright red, soft and velvety to the touch, and are, as a rule, connected with the navel by slender pedicles, and in appearance resemble red currants; occasionally they are sessile.

These tumors are composed of unstriped muscle fiber, mucous membrane, Lieberkühn's follicles, and columnar epithelium, collected into a mass. Typical cases have been carefully described by many observers.

In rarer cases the umbilicus is occupied by a cyst, which may project externally or internally. Such a cyst is lined with mucous membrane furnished with villi, columnar epithelium, and follicles. A cyst of this character is easily confounded with the sac of an umbilical hernia.

The histology and position of pedunculated tumors and sessile cysts at the navel indicate the structure from which they arise—viz., a remnant of the vitello-intestinal duct which, in the embryo, traverses this part of the abdominal wall.

In transverse sections of the umbilical cord, close to the belly wall of the embryo at the fifth month, the vitello-intestinal duct can often be detected, with its lumen lined with sub-columnar epithelium. It is also well known that the duct, instead of shrivelling, sometimes grows equally with the gut with which it is connected, and acquires a lumen almost equal to that of the ileum. Instead of persisting from the gut to the navel the duct may atrophy, leaving a small portion attached to the intestine or to the abdominal wall. Such remnants may develop into cysts the walls of which are identical in structure with those of small intestine.

A much rarer variety of cyst arising in a remnant of the vitello-intestinal duct is due to the distention of that portion of the duct which is connected with the ileum. In recently hatched chicks the intestinal attachment of the duct is often indicated by a nipple-like process on the free border of the gut. This is hollow, but does not communicate with the lumen of the ileum. As a rule, it atrophies completely. It may, however, grow and form a large cyst.

Cysts of identical origin have been recorded in the human subject. One of the best-known cases was reported by Roth.

Occasionally a persistent vitello-intestinal duct will remain open at the umbilicus and discharge feces. Such cases have been successfully dealt with by surgeons.

Cysts of the Urachus.—The urinary bladder of man, in common with that of other mammals, presents at its apex an impervious cord that passes to the umbilicus. This cord, known as the *urachus*, is traversed at birth by a narrow canal lined with epithelium directly continuous with that of the bladder.

The urinary bladder with the urachus is the persistent portion of the allantois, the organ which in the early embryo conveys blood-vessels from the aorta to the developing placenta. In the adult the urachus lies in the subperitoneal tissue exactly in the middle line of the anterior abdominal wall, between the summit of the bladder and the umbilicus. When the urachus becomes dilated it forms a cyst lying outside the peritoneum and in close relation with the bladder.

Instead of a portion of the allantois narrowing to form a urachus, the whole of its intra-abdominal portion may dilate and form a large urinary bladder.

Several cases are known in which the umbilical end of the urachus has remained patent, so that urine was voided at this spot. A urinary calculus has been extracted from such a persistent urachus.

Cysts of the dimensions of a cherry are not uncommon in the urachus, especially near the summit of the bladder; sometimes a number of small dilatations occur, causing the urachus to assume a moniliform appearance.

In rare cases the urachus may dilate into a cyst as large as a distended bladder. The walls of such cysts are composed of unstriped muscle tissue. Care must be taken not to confound a sacculus at the apex of the bladder, or extending into the suspensory ligament, with the cyst arising in the urachus.

Lawson Tait drew attention to the probable origin of some forms of extraperitoneal cysts in the urachus, and the whole matter has been subjected to a very critical and painstaking analysis by Doran.

Allantoic (urachus) cysts not only occur in man, but I have observed them also in the pig, horse, ox, and mole.

Cysts Associated with Remnants of the Mesonephros.—It is well established that in the embryo the mesonephros is closely associated with three organs—the testis, ovary, and kidney. It is also a fact that in at least two situations—viz., in the ovary and in the testis—remnants of the glandular elements of the mesonephros may be occasionally met with in the adult. Many of the tubules of the mesonephros and its duct serve in the male as excretory ducts for the testis, but in the female they persist in a vestigial condition as the parovarium and Gärtner's duct.

There is abundant evidence for the belief that many cysts connected with the testis, ovary, parovarium, and vagina arise from vestiges of the mesonephros and its excretory canals. It will be convenient to begin the description of these cystic conditions by considering those which arise in vestiges of the glandular portion of the mesonephros in the *female.*

Cysts of the Paroöphoron.—For convenience the cysts have been described in the section concerned with ovarian dermoids.

Parovarian Cysts.—The parovarium consists of a series of narrow tubules situated between the layers of the mesosalpinx and closely associated with the paroöphoron. It is easily seen, when the mesosalpinx is stretched and held between the eye and the light, as a series of tubules radiating from the ovary to join a longitudinal tubule situated at a right angle to them. Although the tubules converge as they approach the ovary, nevertheless they remain distinct. Each tubule ends blindly, and is usually lined with epithelium. In form, size, and disposition they resemble the arrangement of the vasa efferentia of the testis. This resemblance was observed by Rosenmüller, who discovered this structure in 1801, while prosecuting anatomic researches at Erlangen. The parovarium is homologous with the vasa efferentia and epididymis of the testis, for these tubular structures in the male and female are the persistent excretory ducts of the Wolffian body (mesonephros). In the female they are vestigial, whereas in the male they are functional.

When present in its typical condition, the parovarium consists of three parts: an outer series of tubules, free at one extremity, known as Kobelt's tubes; an inner set, termed the vertical tubules; and a larger tube running at right angles to the vertical tubules which may occasionally be traced downward to the vagina. This is Gärtner's duct; it corresponds to the vas deferens in the male. The parovarium contains, as a rule, twelve tubules; sometimes as many as seventeen may be counted, and in other specimens as few as five.

The cysts that arise in the parovarium are of two kinds. The more frequent ones are small pedunculated cysts connected with Kobelt's tubes. They rarely exceed a pea in size, and do not call for much comment, as they are of no clinical importance. They need to be mentioned, however, because they are often confounded with the hydatid of Morgagni. Occasionally some of the vertical tubules will break loose and form pedunculated cysts. Should the cyst rupture, it may be converted into a tuft of fimbriæ. The more important cysts are sessile, and remain between the layers of the mesosalpinx. In the early stages it is easy to demonstrate the relation of these cysts to the parovarium. When such a cyst enlarges, it burrows between the layers of the mesosalpinx and makes its way toward the Fallopian tube, which becomes stretched, because the abdominal end of the tube is fastened firmly to the ovary by the tubo-ovarian ligament, and the ovary in its turn is attached to the side of the uterus. In a very large cyst the Fallopian tube becomes greatly elongated, and attains a length of 40 cm. In spite of this extreme stretching, the lumen of the tube is rarely obstructed, and its abdominal ostium can usually be found, the fimbriæ being indicated by a few wattle-like processes.

Small cysts are, as a rule, transparent, but when they exceed the size of a cocoanut, this transparency is lost, and the walls become thick and tough. Small parovarian cysts are lined with columnar epithelium, which is sometimes ciliated; in cysts of moderate size the epithelium becomes stratified, and in large cysts it atrophies from pressure.

The fluid they contain is limpid and slightly opalescent; specific gravity 1002 to 1007, reaction slightly alkaline. A substance, precipitated by alcohol, is present in large quantity.

In big cysts the fluid is often turbid and may contain cholesterin. When parovarian cysts rupture into the cœlom (peritoneal cavity) the fluid is quickly absorbed and excreted by the kidneys.

The points which enable a large parovarian cyst to be distinguished from an oöphoronic cyst are these: (1) The peritoneal coat is easily stripped off; (2) the ovary is usually found at the side of the cyst; (3) the cyst is usually unilocular; (4) the Fallopian tube is stretched over the cyst, but does not communicate with it (Fig. 233); (5) the specific gravity of the fluid does not exceed 1010, and may be much lower; (6) in some specimens the tissue of the mesosalpinx is greatly thickened.

It was formerly believed that cysts originating in the parovarium rarely exceeded the size of an orange, but in 1873 Dr. Bantock demonstrated that parovarian cysts may attain very large proportions, and be capable of containing several liters of fluid. The largest parovarian cyst which has yet come under my care contained 20 liters of turbid fluid.

The age at which parovarian cysts occur is of some interest. It has already been mentioned that cysts of the oöphoron are encountered at any period, from fetal life up to extreme old age. The occurrence of a parovarian cyst has not, as far as I am aware, been recorded in an individual before the age of sixteen; many undoubted cases have been observed at seventeen, eighteen, and nineteen, the cysts being large enough to rise above the pubes. Before sixteen the parovarium appears to be quiescent, but on the advent of puberty it seems to undergo great stimulation; a very large proportion of cysts, generically classed as ovarian, removed between the ages of seventeen and twenty-five arise from it.

It is difficult to come to any satisfactory conclusion as to the relative frequency of parovarian cysts as compared with cysts of the oöphoron and paroöphoron until operators become less casual in their use of the term "ovarian cyst." With our present knowledge they form about 10 per cent.

Parovarian cysts do not often contract adhesions, even when they suppurate. The layers of the mesometrium stretched over them occasionally contain an unusually large proportion of unstriped muscle fiber; they rarely suppurate. Like other forms of cysts and tumors related to the ovary, they are liable to axial rotation and complete detachment.

Epithelium.—It was formerly the custom to believe in the immutability of epithelium; hence many writers have relied upon the characters of the epithelial lining of cysts as indicative of their origin. Mutation of epithelium has been proved so often that it is needless to do more than mention that in some parovarian cysts ciliated cells will be found; in others simple cubical; and in many large cysts no epithelium can be detected. Undoubted parovarian cysts sometimes present low, flat-topped warts.

Gärtnerian Cysts.—A larger experience of ovarian and parovarian cysts has served to convince me that many papillomatous cysts have an origin independent of the paroöphoron. A careful study of the relations of these cysts shows that many of them burrow deeply by the side of the uterus, and even extend along the wall of the vagina.

It is known that Gärtner's duct occasionally persists in women, and after leaving the parovarium it traverses the layers of the mesometrium and runs down the side of the uterus to reach the vagina. As it approaches the cervix, it is often embedded in its tissue.

Evidence is slowly accumulating in support of the opinion that some papillomatous cysts of the mesometrium, especially those which burrow deeply by the side of the uterus, arise in persistent portions of Gärtner's duct, near its termination. Cysts arising in the lowest segment of this duct occasionally bulge into the vagina.

Cysts Associated with Vestiges of the Mesonephros and Its Ducts in the Male.—Cysts arising in the vestiges of the mesonephros (Wolffian body) and its tubules in the male are of two kinds: (1) Encysted hydrocele of the testicle, and (2) general cystic disease of the testicle.

Encysted Hydrocele of the Testicle.—In order to appreciate the nature of encysted hydroceles we must consider a few points connected with the development of the testicle. This gland is very complex, for its ducts, the vasa efferentia, epididymis, and vas deferens, were originally the excretory ducts of the mesonephros (Wolffian body). A study of the evolution of the male secretory organ of vertebrates indicates clearly enough that the ducts have undergone a change of function, and that their relation to the testicle is secondary. An examination of the embryonic testis shows that remnants of the mesonephros persist among the ducts, and only a few of the Wolffian tubules are utilized by the testicle.

In the adult testis a few of the Wolffian tubules become the vasa efferentia, the remainder usually atrophy, but in many individuals one, two, or more persist, usually as pedunculated cysts of small size at the top of the testicle.

The shrunken remains of the mesonephros (Wolffian body) sometimes persist as a collection of cecal tubes furnished with epithelium, lying among the vasa efferentia, between the epididymis and the testis, and often extending a little distance into the tissues of the cord. These remnants are known as the paradidymis. Thus in the male the *mesonephros* is represented by the paradidymis, its *tubules* by the vasa efferentia and Kobelt's tubes, and its *duct* by the epididymis and vas deferens.

The cysts to which the term encysted hydrocele of the testicle should be applied arise sometimes in the vasa efferentia of the testis and sometimes in Kobelt's tubes, and it is a curious fact that these cysts arise in those structures which in the female give rise to parovarian cysts. As encysted hydroceles in the male and parovarian cysts in the female arise in homologous organs, these cysts are morphologically homologous.

Encysted hydroceles are always closely associated with the testis, and lie outside its tunica vaginalis, but they may project into the cavity of this sac. Occasionally a hydrocele of the tunica vaginalis is associated with an encysted hydrocele.

When an encysted hydrocele is very large it may so overlap the testis that it is difficult to differentiate between it and a hydrocele of the tunica vaginalis, until actual dissection in the course of an operation shows that the cyst is independent of the tunica vaginalis.

The lining epithelium of these cysts may be of the stratified, cubical, columnar, or even of the ciliated variety; the cysts contain fluid, which may be clear, or white like milk, due to the presence of fat; sometimes spermatozoa are present, hence they are sometimes called *spermatoceles*, or the fluid may be blood-stained. In size these cysts vary greatly. As a rule, they do not exceed the dimensions of an egg, and often are much smaller.

An encysted hydrocele must not be confounded with a cyst arising in an unobliterated funicular process.

In addition to the sessile form of encysted hydrocele of the testis there is a pedunculated variety which is usually described as a supernumerary hydatid of Morgagni. These cysts rarely exceed a cherry in size, and arise in Kobelt's tubules. As a rule, only one cyst is present, but two or three are not uncommon. Sometimes they will, like the hydatid of Morgagni, project into the cavity of the tunica vaginalis.

General Cystic Disease of the Testis.—This interesting condition has been considered in the section dealing with ovarian dermoids.

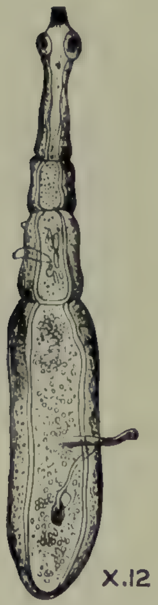

FIG. 241.—TÆNIA ECHINOCOCCUS (Leuckart).

Echinococcus Disease.—*Tænia echinococcus*, a tapeworm which in its mature form inhabits the intestines of dogs, is about 4 mm. in length and consists of four segments, of which the fourth is larger than the rest of the body and is the only segment that becomes mature (Fig. 241).

It has been calculated that a ripe proglottis of *T. echinococcus* contains about 5000 ova. This is a good example of the prodigality of nature in all that concerns eggs, both animal and vegetable.

The eggs of this worm are passively conveyed, either with raw vegetables, uncooked food, or water, into the alimentary canal of man, where they are hatched; the embryos migrate from the intestine into some vascular organ or tissue, or by gaining entrance into a blood-vessel, are passively conveyed into some distant part of the body and become transformed into cysts.

The multiplicity of the lesions depends on the number of the ova swallowed, and the extraordinary number of the cysts and colonies in some patients would suggest that an entire proglottis had been ingested.

The cyst-wall has a peculiar structure (Fig. 242); it consists of an external, highly elastic, lamellar cuticle, and an internal lining consisting of granular matter, cells, muscle tissue, and a water-vascular system.

The inner lining is often referred to as the parenchymatous layer. In addition to the proper tissues of the cyst, there is often a more or less complete fibrous capsule, especially when the cyst projects into the peritoneal cavity.

The true cyst is maintained in apposition with the fibrous capsule by the pressure of the contained fluid; when this is removed by the abstraction or escape of the fluid, the mother-cyst at once collapses.

The fluid is clear, limpid, colorless or slightly opalescent; specific gravity 1004 to 1015; contains chlorid of sodium, no albumin, succinic acid, and occasionally, in hepatic cysts, leucin, tyrosin, and sugar. Hooklets and scolices are also found.

When the cyst attains the size of a walnut, small vesicles or *brood-capsules* develop from the parenchymatous layer. These brood-capsules develop numbers of heads or *scolices*. The scolex when fully developed is about 0.3 mm. long, is furnished with four sucking discs and a rostellum of tiny blunt hooklets; it has a water-vascular system and numerous calcareous particles. The fore-part of the scolex can be withdrawn into the hinder part; indeed, this is the position in which they are usually found (Fig. 243). The scolex represents the head of a tapeworm, and when ingested by a dog becomes mature.

As fresh brood-capsules and scolices are formed, the cyst enlarges, and, when seated in an organ or cavity of the body which imposes little restraint upon its growth, it may attain enormous proportions; for example, echinococcus cysts of the liver have been known to acquire a capacity of sixteen pints. In many *daughter-cysts* are formed from brood-capsules and probably from scolices. Cysts containing these translucent thin-walled vesicles are known as *echinococcus colonies*.

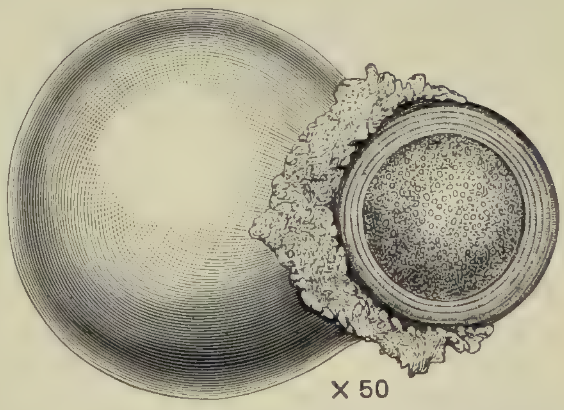

FIG. 242.—AN ECHINOCOCCUS CYST SHOWING THE PECULIAR LAMINATION OF ITS WALLS (Leuckart).

Occasionally echinococcus cysts even of large size do not contain vesicles or brood-capsules; such are said to be *sterile*, but their walls exhibit the characteristic lamination, and this enables the nature of the cyst to be recognized in otherwise doubtful cases.

An exceptional mode in which this disease manifests itself is known as *Echinococcus multilocularis* (Virchow). In this condition the vesicles are of small size, but occur in great number, and are not contained in a mother-cyst. The vesicles in such cases rarely exceed a pea in size, but the majority are much smaller; very many are no larger than millet-seed or rape-seed. This variety occurs most frequently in the shafts of long bones. They have also been observed in the spinal canal.

The multilocular form also occurs in the liver as a firm tumor, which on section presents trabeculæ of dense fibrous tissue that cause it to assume an alveolar appearance. The alveoli contain a gelatinous substance in which the shrunken vesicles are embedded.

Most of these minute vesicles are sterile, but with patience here and there a few hooklets can be demonstrated. Virchow was the first to demonstrate the parasitic origin of such tumors in the liver; previously they had been described as colloid cancer. In very rare instances contracted and shrunken vesicles embedded in gelatinous material and surrounded by a distinct cyst have been observed in the liver. No satisfactory explanation has yet been advanced to account for this curious variation in the development of the parasite. Ziegler has written an exhaustive monograph on this form; he considers it a distinct species, and has met with it in the brain, lung, and liver.

The usual mode of termination of an echinococcus cyst is to cease to grow; it then dies, shrivels up, and calcifies, assuming a friable appearance like old mortar.

When the cyst continues to grow its tendency is to rupture; the great tension exerted by the accumulating fluid, and especially the formation of daughter-cysts, induces necrosis of portions of the cyst-wall.

When these cysts are contiguous to hollow viscera, such as the intestine, stomach, trachea, and the like, their walls are apt to come into contact with them, and the mutual pressure leads to absorption of the intervening tissue, and allows of the transmission of gas, air, or the osmosis of fluids which kill the parasite, and the entrance of pathogenic microörganisms establishes suppuration.

In many instances the communications between the cysts and hollow viscera are so free that the contents of the cyst are evacuated. In some instances this is a fortunate termination; but frequently it is a catastrophe to be dreaded, as it may immediately cause death, or lead to secondary changes that have ultimately a fatal issue.

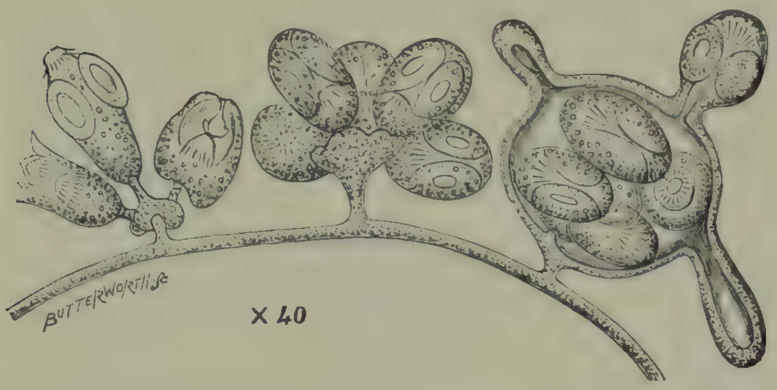

Fig. 243.—Portion of the Cyst Wall of an Echinococcus Colony Showing Scolices (Leuckart).

In rare cases the vesicles in a colony become converted into colloid material of about the consistence of gelatin.

Geographically, *T. echinococcus* has a very wide distribution; which corresponds with that of the dog. It is, however, far more frequent in some regions of the world than others. Iceland is notorious for the frequency with which its inhabitants are infected by this parasite. After allowing great latitude for errors in the direction of excess in calculating its frequency, hydatid disease must be regarded in the light of a persistent epidemic so far as that island is concerned.

Next to Iceland, Silesia is usually regarded as the most infected district in Europe. In Australia the disease is very prevalent; in Asia it is known. In America the disease is not frequent, and judging from the few references to it in American literature, this disease appears to be rarer in North America than in the British Isles.

Topographic Distribution.—Although an echinococcus cyst may arise in almost any organ or tissue of the human body, it shows an obvious partiality for certain tissues. A comparison of statistical tables shows that these cysts occur more frequently in the liver than in all other parts of the body together; while in other organs, such as the breast, thyroid gland, or spinal cord, the literature of a century would probably furnish less than a score of trustworthy records.

It is necessary to point out in regard to the distribution of echinococcus colonies that though on superficial examination they may appear to be lodged in the liver, kidney, uterus, or rectum, a closer and more critical inquiry shows that in nearly all instances the parasite selects the loose subserous tissue. For example, echinococcus cysts in the liver usually lie in the tissue beneath the peritoneum covering this organ. This is certainly true of the uterus, and a few cases reported as growing from the Fallopian tube or ovary are really cases of infection of the loose connective tissue of the mesometrium. In the case of the kidney the parasite flourishes in the connective tissue of the renal sinus.

Echinococcus cysts occur singly or may be distributed over the body in great numbers. The effects to which they give rise vary with their situation and size. A cyst of such a size as to cause death from mechanical causes when lodged in the spinal cord or heart, would produce no inconvenience in the liver or great omentum. An echinococcus colony on the under surface of the liver will often attain a large size before causing inconvenience to the patient, whereas one only half its size situated in the pelvis will produce distress by interfering with the function of the rectum or bladder. On the other hand, a small colony in the liver no larger than an orange when accidentally ruptured and its contents escaping into the peritoneal cavity may rapidly destroy life by bleeding, but a cyst the size of a melon, or larger, bursting into the rectum will not lead to much trouble; even a small cyst so seated as to rupture into the trachea will, when the event comes to pass, almost inevitably cause death by suffocation. Indeed,

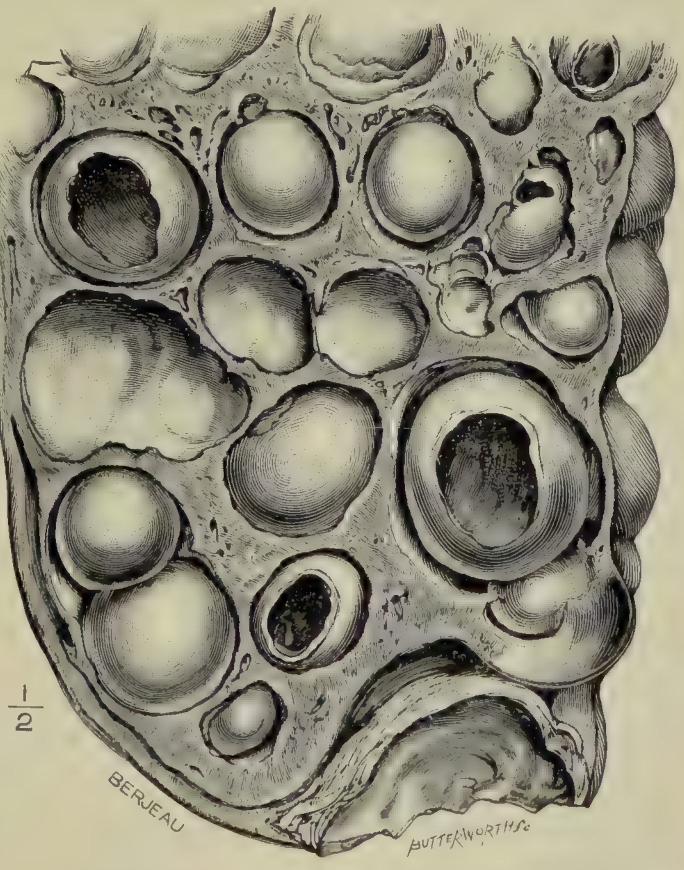

Fig. 244.—Portion of a Liver which Weighed 25 Pounds thoroughly Infested with Echinococcus Cysts.

the ways in which echinococcus colonies kill are so many and so various that they will be dealt with under each organ.

Rupture of a large colony into the abdomen may lead to general infection of that cavity, the brood-capsules engrafting themselves on the peritoneum and producing an appearance like miliary tuberculosis.

Liver.—Echinococcus cysts are more common in the liver than in any other organ; the frequency with which they occur in the liver as compared with other viscera is not due to any selective power on the part of the echinococcus embryo, but may be attributed to the fact that it finds its way into the tributaries of the portal vein and is passively conveyed into the gland. As a rule, the cysts occur singly in the liver, but many instances have been reported in which three or four have been present; but there is apparently no limit to their number. The museum of St. Thomas' Hospital, London, contains a liver removed after death from a sailor; a section of it is represented in Fig. 244 to show the distribution of the cysts. A careful examination of this specimen shows that in this instance the parasites invaded the loose connective tissue in which the hepatic vessels and ducts are embedded. In the usual course the parasites make their way into the loose areolar tissue lying beneath the peritoneal investment. Leuckart found, in his feeding experiment on pigs, that the embryo had a preference for the loose tissue in this situation.

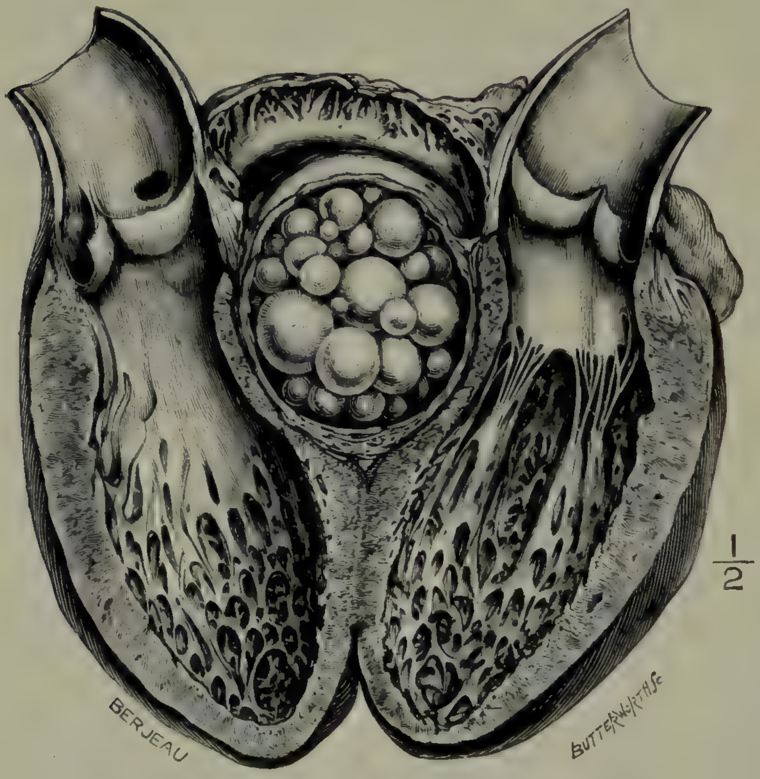

FIG. 245.—A HEART LAID OPEN TO SHOW AN ECHINOCOCCUS COLONY IN THE INTERVENTRICULAR SEPTUM.

The relative frequency of echinococcus cysts in the liver, the large size they attain, and the risks they occasion to life have caused them to be carefully studied.

When the cyst ruptures spontaneously it takes various directions; it may burst into the abdomen, or into the pleura or lung and the vesicles escape through the bronchial tubes and trachea. Rarely it may burst into the pericardium, the stomach, the intestines, or rarely into the gall-bladder, and still more rarely into the vena cava, when the contents will be carried as emboli into the right cavities of the heart. When the fluid escapes into the abdomen it sets up an urticaria which itches intensely.

The Heart.—In this organ echinococcus colonies are not rare. I have recently made a careful study of this matter and find that the parasite selects the loose areolar tissue of the auriculo-ventricular groove and then bulges into the adjacent cavities.

The colonies may cause death by hampering the action of the heart or by bursting into the adjacent auricle or ventricle, the vesicles and membrane being conveyed as emboli into the pulmonary or the systemic circulation.

The Lungs.—Echinococcus cysts occur in the lungs under two conditions.

1. The cyst (for it is usually single) may be situated wholly within the lung, and in most cases chooses the lower lobe, especially of the right lung.
2. It grows in the tissue immediately beneath the pulmonary pleura and projects as an outgrowth from the lung into the pleural cavity.

Small cysts occasion little inconvenience, but increasing in size they compress the lung and lead to hemoptysis. Apart from the mere pressure effects produced by the cyst, it is liable to rupture into a bronchial tube, and pieces of membranes and vesicles being coughed up reveal the nature of the case. When the cyst communicates with a bronchus suppuration is the consequence. It is well to bear in mind that because vesicles and membrane are coughed up it does not necessarily follow that the colony is in the lung, for echinococcus colonies in the liver are sometimes evacuated by this route.

Pancreas.—An echinococcus colony in this gland is very rare. In a case under my care the cyst was opened and drained, as its enucleation was impracticable. The patient, a woman, died four weeks later from hemorrhage due to ulceration of the inferior pancreatico-duodenal artery.

Kidney.—Many examples of a primary echinococcus colony in the kidney have been recorded; it may arise in the loose connective tissue which fills the renal sinus, or grow immediately beneath its capsule. In both situations a cyst may attain a large size. When small, they rarely cause trouble or inconvenience, and their existence is only known in the course of a post-mortem examination.

There are good reasons for the belief that a colony in the kidney may rupture into the renal pelvis, the fluid and vesicles passing down the ureter to be discharged by the urethra. This is a very satisfactory though painful mode of termination.

Echinococcus cysts are met with, though rarely, in the *thyroid gland* and even in the *adrenal*.

In the *mammary gland* a fair number of cases have been observed and carefully recorded. In some instances a colony has existed for ten years without producing inconvenience. A cyst in this gland may attain the dimensions of a child's head.

In countries where this parasite is rare, the disease is rarely diagnosed. Colonies may arise in the subcutaneous tissue in any region of the trunk, head, or limbs. Many have been observed in the orbit.

Uterus.—Echinococcus colonies have on several occasions been observed growing beneath the peritoneal investment of the uterus and forming a pedunculated tumor resembling clinically an ovarian or a subserous fibroid, but commonly the seat of infection is the loose connective tissue of the mesometrium, and the cysts as they enlarge involve the uterus, Fallopian tubes, bladder, and rectum. In many cases the disease forms part of a general invasion of the subperitoneal tissue; in exceptional instances the cyst may be solitary and simulate in its mode of growth a parovarian cyst, or it may have the ovary stretched over part of its circumference and resemble an ovarian cyst. A critical examination of reports of cases and of specimens supposed to be examples of primary echinococcus cysts of the ovary show them to be instances in which the cyst arose in the mesometrium and involved the ovary secondarily.

In one remarkable instance a colony 11 cm. in diameter grew beneath the serous covering of the uterus and opened into the right Fallopian tube, which was greatly distended, thrown into convolutions, and stuffed with vesicles (Maloney).

Brain.—Echinococcus cysts occur in connection with the meninges of the brain; the loose tissue of the pia mater is favorable for their development, but they are usually sterile and lack the thick fibrous capsule which surrounds them when lodged in the liver or omentum.

Bones.—Echinococcus colonies are very rare in bones, and they seem to prefer the medullary cavities of long bones; the variety found in the bones of man is that known as *Echinococcus multilocularis*, in which there is no mother-cyst, but the medullary cavity of the bone is occupied by a multitude of vesicles. The effect of these colonies on the bone is very extraordinary; they induce atrophy of its shaft, and at length the bone breaks from some trivial injury. In some instances operations have been undertaken for the relief of abscesses supposed to be due to necrosis, and when the bone has been opened up vesicles have escaped. When the colony occupies the end of a bone, the vesicles may invade the adjacent joint.

The Spine.—Echinococcus cysts occur in connection with the spine under three conditions.

1. *The cysts are situated entirely within the canal.* Such cases are divisible into two sets: (*a*) Those inside the dura mater, and (*b*) cysts lying in the loose connective tissue between the bone and dura mater. In the majority of cases the cyst, though situated within the neural canal, is external to the theca. Schlesenger tabulated the variety and position of four hundred tumors of the spinal canal; he found that of this number forty-four were echinococcus cysts. Five were intradural and thirty-nine extradural.

2. *The cysts arise in a vertebra and extend into the neural canal.* Primary echinococcus colonies of the vertebræ are of the multilocular variety.

3. Echinococcus colonies growing in tissues adjacent to the spine may involve the vertebræ and extend into the spinal canal.

Symptoms and Diagnosis.—These will entirely depend on the situation of the disease. For example, when the cyst is in the spinal canal the symptoms will be those common to any tumor large enough to compress the cord and produce paraplegia. In the cranial cavity the localizing signs are those presented by all tumors which compress the brain.

In the abdomen especially when the cysts are connected with the liver the nature of the swelling may be suspected when it is painless, slowly increasing, and especially if a peculiar vibratory thrill is produced by percussing the middle finger of the left hand when it is laid firmly over the tumor.

When the colonies burst into hollow viscera and the characteristic vesicles are discharged by the bowel, urethra, vagina, trachea, or through suppurating sinuses, then the nature of the disease is self-evident. In countries where echinococcus disease is endemic it is usual in cases where a tumor or swelling exhibits negative characters to regard it as an echinococcus cyst. More than half the examples of this disease occur as surprises in the course of surgical operations.

Treatment.—This is always surgical, and the particular method of carrying it out varies with the situation of the cyst. When they hang as big as apples from the omentum, it is only necessary to expose the cysts through an incision in the belly wall, ligate the pedicle, and remove them. In many cases they are firmly adherent to surrounding structures. In these circumstances the fibrous capsule should be freely incised and the mother-cyst enucleated; the empty capsule rarely gives trouble. Suppurating cysts demand free incision and drainage.

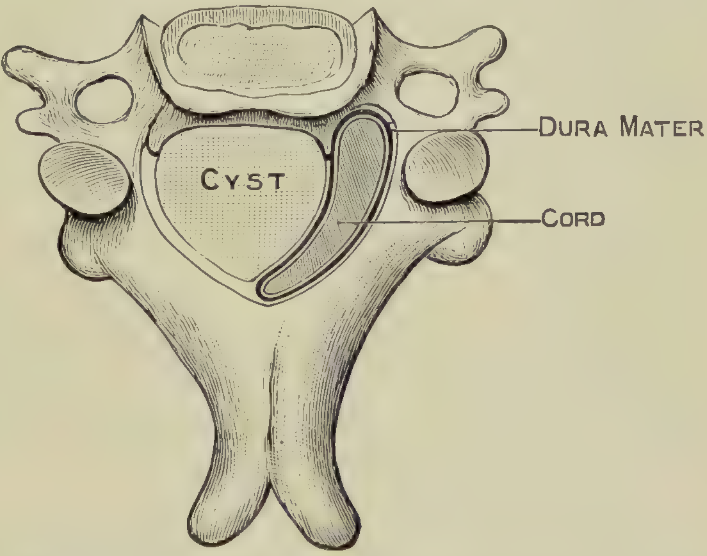

FIG. 246.—AN EXTRADURAL ECHINOCOCCUS CYST COMPRESSING THE CORD AT THE LEVEL OF THE THIRD CERVICAL VERTEBRA (after Colman).

In removing colonies it is wise to avoid soiling the edges of the wound with brood-capsules, for there are reasons for believing that they may give rise to cysts of some size in the cicatrix.

In the case of the *liver* echinococcus colonies treated by incision, enucleation of the capsule, and free drainage give but little trouble. Great care should be taken thoroughly to remove the mother-cyst, for decomposition of this tissue when left is a source of grave danger. All meddling methods—as punctures with trocars, aspirations, and electrolysis—cannot be too strongly condemned.

Echinococcus cysts in the *lungs* require to be treated on the principles of empyema, and in this situation Lendon particularly insists on the necessity of removing the mother-cyst.

The contents of dead colonies are sometimes so firm that they require removal with a scoop. When the cyst wall is calcified it often leads to a persistent sinus.

In the case of *bones* the treatment consists of incision, evacuation of vesicles, and drainage. Exceptionally, when the bone is seriously damaged, fractured, or a large joint invaded, amputation has been found a necessity.

Echinococcus cysts within the *cranium* have been localized, exposed by trephining, and after evacuating the fluid the cyst has been successfully extracted (Verco; Rennie and Crago; Mills and MacCormick).

Echinococcus cysts in the spinal cord have been successfully submitted to surgery (Tytler and Williamson).

Single echinococcus cysts and colonies give, as a rule, admirable results when treated surgically, but in cases where the patient suffers from a general infection the disease is very inveterate and demands much persistence on the part of the surgeon, and calls for great courage and fortitude on the part of the patient.

CHAPTER XXII.

WOUNDS AND CONTUSIONS.

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I. WOUNDS.

A wound is a forcible solution of continuity of tissue. The physical characteristics of wounds are determined mainly by the physical quality, the angle of incidence, and the velocity of contact of the substance causing them, as well as the nature and quality of the tissue involved.

The division of tissue with a minimum of contusion by means of the sharp edge of a hard substance—as, for example, a surgeon's knife—constitutes an *incised* wound. The division of tissue with a maximum of contusion by means of a substance having a blunt edge or a flat rough surface, such as blows by a club, causes a *contused* wound. A rough, irregular division caused by a tearing or dragging force, such as the teeth and claws of animals, constitutes a *lacerated* wound. A wound whose physical qualities may be either incised or contused, but whose leading characteristic is depth, constitutes a *penetrating* wound. A wound presenting a minimum of division and a maximum of penetration and of spreading of tissue, caused by such objects as tines of forks, needles, thorns, etc., is a *punctured* wound. A wound passing through hollow viscera, as a gunshot wound of the intestines, is a *perforating* wound. A mere surface solution of continuity, as from surface contact in an extremely obtuse angle of incidence with velocity, such as may be incident to sliding or coasting, is an *abrasion.* A linear solution of continuity, usually from stretching, such as may be caused by a divulsion of the sphincter ani, is a *fissured* wound. A wound caused by friction of sufficient intensity to generate a burning degree of heat as well as abrasion, such as may be caused by sliding down a rope while sustaining the weight with the grasp of the hands or by the contact of swiftly moving belting of machinery, causes a combination of a burn and an abrasion, and may be designated a *brush burn.*

As to the relation to the body surface, a wound involving the skin or mucous membrane is an *open* wound; those limited to the tissue underneath, as the rupture of muscles or tendons, the fracture of bones or the laceration of the soft parts by their fragments, may, according to their location, be classified as *subcutaneous* or *submucous* wounds.

When deleterious chemical substances, such as the venom of snakes, enter, it becomes a *poisoned* wound. When active pathogenic organisms are introduced, it becomes an *infected* wound.

A wound of any physical or pathologic variety involving the rupture of important blood or lymphatic vessels, the injury of nerve-trunks or of important viscera, may be designated a *complicated* wound. When the edges of a wound made across the direction of the natural folds of the skin are drawn more or less apart it may be designated a *gaping* wound.

Finally, there may be every variety of combination of the foregoing; a single wound may be described as lacerated, contused, poisoned and infected, etc.

Phenomena Attending Wounds.—The immediate phenomena attending a wound depend upon its variety, its location, and the mental and physical quality of the patient. Among the more common immediate phenomena of simple wounds are *pain, hemorrhage, swelling,* and *discoloration.*

Pain.—When the incidence of contact is at a high velocity—as, for example, a modern army rifle shot in fair range—there may be little or no pain, and the wound may be discovered by the sight or the sensation of trickling blood, while a low velocity of incidence, as in pinching a finger in a door or having one's toes stepped upon, causes great pain. Likewise, complete destruction, as in the separation of a limb by the trucks of a railway train, may cause little pain, while the partial destruction of the end of a finger by a misdirected blow of a hammer may produce intense pain.

Incised and punctured wounds usually cause less pain than contused and lacerated. Some tissues and organs, such as the testicles, pit of the stomach, tip of the nose, nerve-trunks, and abdomen, have not only special but exalted pain-producing qualities, such as "sickening," "cramping," "tingling," etc.

There are very marked individual as well as national characteristics which modify pain. The phlegmatic bear pain better than the highly nervous. The wound of the obstetric forceps probably causes no pain to the infant whose sensorium is not yet physiologically connected with the periphery. Likewise, the blunted sensibilities measurably protect old age from the more acute pain of wounds.

The Orientals are reputed to be less susceptible to pain than the Occidentals.

The psychic factor is important. In the heat of battle soldiers may walk uncomplainingly upon the naked fragments of their legs. At the height of their religious fervor Dervishes may inflict severe injuries without pain. In the cataleptic, the hypnotic, and kindred states pain may be abolished.

The state of the tissue is important. Inflamed tissue and tissue subjected to repeated irritation are more susceptible to pain. An injury in parts exposed to extreme cold is more painful than a like injury in a higher temperature.

Among the local conditions which influence pain after the immediate traumatic effects have passed away tension is the most important. Whether due to subcutaneous hemorrhage, to edema, or to interference with the return circulation, tension may cause pain varying from that of an uncomfortable sensation to an unbearable throbbing. Infected wounds become progressively painful until either resolution, abscess with free discharge, or total gangrene is reached.

Hemorrhage.—In virtually all wounds there is hemorrhage. If a large artery is involved, the hemorrhage will be in jets. If quite small, it may be continuous and red, or there may be rhythmic modification. An exception to this color would be the arterial hemorrhage in asphyxia. When the walls of veins are involved the hemorrhage will present a steady stream of dark blood; if capillaries, there will be oozing of red blood.

With reference to the time elapsed hemorrhage may be classified as immediate, occurring at the time of injury; consecutive, occurring a few hours to twenty-four hours later; and secondary, when vessels are opened by the destructive process of inflammation.

Hemorrhage into the substance of an organ may be designated parenchymatous; when into the hollow viscera or cavities of the body—*e. g.*, the abdomen—as internal; when in the tissues of the extremities or walls of the trunk, subcutaneous. Hemorrhage from large venous trunks causes a most marked effect upon the circulation, because the amount of blood that would naturally flow to the heart is immediately diminished.

The amount of hemorrhage from wounds is determined in part by the general condition of the patient. There may be hereditary or individual tendency to hemorrhage, even in the absence of the state known as hemophilia. Plethora, high blood-pressure, and congestion favor hemorrhage. The local conditions determining hemorrhage are mainly those relating to the peculiarities of the blood-supply of the part, the nature of the tissues in which the vessels run, and the nature of the wound. Wounds in the richly supplied tissues of the face and neck are attended by profuse hemorrhage, while in the scantily supplied tissues, such as tendons, cartilage, and fascia, there is comparatively slight hemorrhage. In the loose connective tissue, such as that of the orbit and scrotum, hemorrhage tends to be progressive, probably because of the absence of elastic restraint.

The determining factor of greatest importance, however, is the nature of the wounding substance. Clean-cut wounds, making a freer opening in the vessel and offering less natural conditions for clotting, are attended by maximum hemorrhage; in lacerated and contused wounds, a minimum hemorrhage occurs. It is rare indeed that the avulsion or the complete crushing of a limb is attended by fatal hemorrhage. This is due, not, as has been supposed, to a retraction of the elastic coat, but to the fact that the elastic coat being more brittle is torn first, while the fibrous coat is drawn out over its end like the threads of the Indian puzzle, then, retracting, closes the lumen, while at the same time this fibrous mesh-work produces the ideal condition for clotting. The retraction of the severed ends of the vessels of the scalp oftentimes conceals a bleeding point. In subcutaneous division of vessels the tissues may become so much separated by the blood as to constitute a dissecting hemorrhage. This is particularly true in injuries of the lower dorsal, lumbar, and sacral region, in which large hematomata frequently form.

Swelling.—Most wounds swell, the minimum appearing in incised; the maximum, in contused. Swelling is due mainly to hemorrhage, transudation, interference with the return circulation both of the veins and lymphatics, and the pouring out of lymph from the divided lymphatics. In loose connective tissue, such as the orbit, swelling is most marked; in dense tissue, as cartilage, tendon, fascia, bone, least so.

Discoloration.—Discoloration is due primarily to hemorrhage. If immediately under the skin, it appears at once; if deep, its first appearance may be noted after several days, as is often noticed in fractures of the femur or humerus. If the hemorrhage is so superficial as to exchange oxygen with the air, the discoloration is red; if too deep for such exchange, black. The progressive changes of hemorrhage are from black to brown, then orange, then gradually fading out.

Wound Secretion.—From all wounds there is a fluid discharge, consisting largely of lymph from the divided lymphatics and serous transudation from blood-vessels.

TREATMENT OF WOUNDS.

The first consideration is the arrest of hemorrhage. In accomplishing this due consideration must be given to the source, whether venous, arterial, or capillary; to its location, whether of an extremity, in loose areolar tissue, in joints, in cavities, in the respiratory tract, or in the brain and spinal cord. If from spurting arteries, they should be isolated and tied. Under certain conditions they may be clamped, when tying is for the moment impossible. If capillary, pressure and cold or hot applications may suffice. If the oozing is extensive and pressure not applicable, control is best secured by suturing the surface, using the buttonhole stitch with needle and catgut. It is well to remember that in capillary oozing the blood-pressure at best is but a few millimeters of mercury. It is only necessary in pressure or in stitching to secure a slight margin of constant pressure above this. Tight suturing is apt to cause strangulation of tissue with lowering of the vitality. The continuous over-and-over suture may miss oozing points between the loops of the stitch. The buttonhole stitch causes pressure in both directions, that is, pressure in the direction of the needle as well as in the direction of the line of sutures, thus putting all the tissue under a certain amount of pressure. In oozing from the urethra, the nose, and other points, adrenalin applied either in free solution or by means of saturated pledgets of cotton may be useful. If the hemorrhage is venous, posture is most important. Striking illustrations of this are seen in hemorrhage from varicose veins of the extremities. As a temporary measure for controlling hemorrhage tourniquets or direct pressure may be used. If the hemorrhage be venous, direct pressure is most effective; if arterial, the tourniquet or direct pressure upon the supplying trunks. Frequently in accident wards one finds admitted patients suffering from free venous hemorrhage from varicose ulcers with tourniquet applied above the bleeding point, causing obstruction to the return circulation, thereby increasing the hemorrhage, whereas elevating the limb and removing the obstruction may be sufficient entirely to relieve it. In hemorrhage in the scrotum the bleeding vessels should be freely exposed and every possible bleeding or oozing point secured and tied. It is always best to make a complete hemostasis, especially when the circulation has been depressed; otherwise, when reaction comes on hemorrhage may recur. The use of chemical agents such as persulphate of iron, and the internal administration of such drugs as ergot, are no longer recognized as surgical procedures. Cauterization, too, need rarely be employed. (For a full consideration of hemorrhage see Surgery of the Vascular System.)

Cleansing of Wounds.—Assuming that all accidental wounds are infected, the cleansing is a matter of first importance. Perhaps the most common error consists in an incomplete cleansing followed by closure by suture or by the application of occlusive dressing, such as adhesive plasters, collodion, etc. This method presents the double danger of retaining infected dirt or débris, and the retention of wound secretion. Such errors more than any other are responsible for severe local and regional inflammations. It is difficult indeed to overstate the importance of correct primary wound cleansing and dressing.

The extent of the primary cleansing and dressing should vary according to the location, the extent and the probable cause of the infection. Wounds should be searched for foreign bodies. In wounds made by glass, knives, or other foreign bodies a close examination to determine whether any tendons, nerves, or other important structures have been divided should be made. If so, they should be immediately sutured. The proximal end of a divided tendon may retract so far as to be extremely difficult to find. This is especially true in wounds of the deep palmar area.

Location.—In wounds of hair-covered areas, such as the scalp, face, armpit, pubes, unless specially contraindicated on cosmetic grounds, as in case of minor wounds of the scalp in women, the field should be widely shaved. In general the wound and the surrounding field should be scrubbed as thoroughly as in preparation for an operation. In children and in areas covered with delicate skin, gauze or cotton should supplant the brush. In this connection it may be stated that the use of coarse brushes capable of abrading the skin is to be deprecated in the preparation of any surface of the body.

If the wounds are minor, cleansing may be easily accomplished without anesthesia; but if more important on account of size or location, it is better to anesthetize fully, thus rendering a more complete cleansing possible. In extensive crushes of the hands or feet this is of special importance. The greatest urgency for anesthesia, thorough cleansing, and exploration of the wound arises in case of injuries inflicted by toy pistols, giant crackers, etc., such as occur on Fourth of July celebrations, in which there exists a possibility of tetanus infection. This point has been especially emphasized by D. P. Allen, in his Lakeside Hospital service.[1] There are certain possible exceptions to the rule of thorough scrubbing. Ore-handlers' extremities are frequently covered with a very fine red powder which is closely adherent to the wound and skin. This fine powder can scarcely be removed by ordinary measures without inflicting serious additional damage to the wound. Some years ago F. E. Bunts called attention to the relative harmlessness of this powder and even found that it possessed distinct therapeutic value as a dusting-powder in certain ulcers and sluggish wounds. In this class of wounds it was found that infection was no more likely and repair was more prompt if restricted cleansing were made and antiseptic dressings applied than if the very irritating process of scrubbing sufficiently to remove the tenacious and almost impalpable iron-ore dust had been resorted to.

Other cases presenting an analogous partial local immunity are those whose occupation covers their hands with grease and oil. This form of dirt is relatively harmless, and, not unlike the ore dust, is most difficult to remove except by the use of a special soap or certain chemicals. The removal of the grimy black oil and grease which has been so thoroughly driven into all the crevices and pores of the skin by the ordinary methods of scrubbing is most difficult, requiring such an amount of mechanical effort as still further to injure the already severely crushed tissue, if the cleansing be carried to the very margin of the ragged, irregular edge. If this edge be spared such scrubbing, a black zone bounds the wound at precisely the place demanding cleansing. In such cases, too, the scrubbing may be superseded by gentle cleansing of the wound proper and the application of moist bichlorid dressings. The use of moist bichlorid of mercury dressings as a routine practice in all lacerated wounds will be found a most excellent and reliable method of treatment, provided that the solution be not used too strong, never above 1:3000, and much weaker on delicate or susceptible skins. This precaution is particularly important when it becomes necessary by reason of infection to keep up the moist dressings for any considerable length of time.

Drainage.—In superficial wounds, especially about the face, in non-penetrating wounds with a relatively small amount of contusion, drainage is not necessary. In wounds involving subcutaneous tissue, such as muscle, fascia, and bone, drainage is always advisable. Depending upon its importance, drainage may consist of rubber tubing, a cigarette drain made by surrounding a strip of gauze or wick with a protective such as rubber, gutta-percha, strips of rubber tissue, or suture-material laid in the wound with the free ends emerging, etc.

In providing drainage, especially in deeper wounds, it is best to make it as nearly dependent as possible, frequently making a counter-opening. Free drainage in many cases is provided by omitting all or part of the stitches, or by placing them loosely and at long intervals. Then, too, drainage is facilitated by not making layer sutures unless it be for the purpose of uniting some important anatomic structure, as a severed muscle.

In fat subjects drainage may be especially required, though this necessity may be obviated in all instances in which care is taken to make a good approximation by light catgut, suturing from the depth of the wound outward. Such sutures if tightly drawn cause local necrosis. Should there be dead spaces which cannot be obliterated drainage should usually be employed. In amputations drainage is required in direct proportion to the infection and the lack of hemostasis. In amputations by the Esmarch bandage and tourniquet methods a certain amount of oozing is likely to follow. If the amputation be made by a serial dissection without tourniquet or Esmarch bandage, each bleeding point secured promptly as it appears, and after all the tissues have been divided and the severance of the limb completed, if the end of each divided muscle is put under a slight pressure by a running catgut suture, but little necessity for drainage exists; a piece of protective inserted at one corner will suffice.

In draining wounds of the brain it is quite important to avoid drainage through the scalp immediately overlying exposed brain tissue on account of the danger of encouraging a hernia cerebri. The drainage should be carried through an opening through the healthy scalp at some distance from the exposed brain.

Drainage of brain abscesses is difficult; the drainage-tube is likely to become displaced. Rubber tubes are probably most serviceable, but they must be securely held in place. This may be accomplished by sewing the tube to the scalp at the point of exit, or by securing it by transfixing it with a large safety-pin, which in turn may be held firmly in place by bandaging. This subject will be elaborated in another chapter.

In draining the pleural cavity especial care must be taken to prevent the displacement of the drainage either wholly out of or into the pleural cavity. Perforated rubber tubes are the best. If irrigations are to be employed, the tube may be double, providing for both inflow and outflow, or there may be two openings through the wall, a higher and a lower.

In draining the abdomen the more common material is gauze alone, or gauze with protective wrapped about it as a cigarette is rolled, known as the cigarette drain, glass tubing or rubber tubing. The Fowler position is often important, as it induces the fluid to gravitate toward the pelvis.

Closure.—Closure of wounds is oftentimes a matter of great importance. Perhaps the point requiring the most careful consideration is that of deciding whether or not any closure should be made. A proper selection of cases for closure must rest largely upon individual experience. One would hesitate to close any wound when the surroundings of the patient are unfavorable and the assistants and the after-care unreliable. In field emergency surgery one would give the benefit of the doubt in favor of leaving the wound open. In a hospital case under favorable surroundings most wounds may in some manner be closed. The probable nature of the infection is a very large determining factor in the decision as to closing. Wounds received in a slaughter-house, meat shop, or dissecting room, one would virtually never close, and wounds made by the teeth of carnivorous animals, infected tools, etc., would best be left open. Likewise wounds made by the teeth of a garden rake or other implement that might carry tetanus bacilli should under no circumstances be closed.

Then, too, the tissue involved is a determining factor; for example, wounds in the palm of the hand and sole of the foot should rarely be closed by sutures at least, while wounds in the richly vascular regions of the face and neck may be closed with safety.

The general health of the patient must also be considered, as in a diabetic subject, or in marasmus or other constitutional states in which the resistance is at a low ebb, in which it would be best not to close the wound without drainage.

Experience in recent wars has taught the military surgeon that uncomplicated penetrating gunshot wounds are best treated by the application of antiseptic or aseptic dressings without drainage. In these instances it has been found that the modern projectile, in passing through nonsterilized clothing and skin, does not carry infection of importance into the deeper parts. At least such infection as is taken in with the bullet is destroyed by the natural resistance of the tissues. It is probable that the aseptic course of such wounds is determined very largely by the condition of the bullet track with reference to the contusion of its wall. The condition of the walls depends upon the shape, size, and velocity of the bullet. In a track but little contused the local resistance is so little impaired that the minimum infection which enters is destroyed. This is probably the most important factor, because it is noted that there is a marked difference between the reaction in wounds that have not been probed as compared with wounds that have been. The presumption is that in the process of probing infection is carried from the outer margin of the wound into its deeper parts. The inadvisability of probing a wound even in modern civil practice, in which the large lead and revolver bullets are used, is almost equally emphatic in cases intended to be treated without drainage.

Methods of Closure.—Having decided on closing the wound, there are many methods available. The most universally employed suture is the *interrupted stitch* of silkworm-gut or silk. Silkworm-gut is the best because it does not absorb moisture and is non-irritating. A needle, preferably with a bayonet point, is entered from without inward one-fourth of an inch from the edge of the wound straight through all layers of the skin perpendicular to the surface; it is then carried to the skin on the opposite edge of the wound and passed similarly from within outward. The ends of the suture are then tied in a square knot, or, if there be undue tension, with a surgeon's knot, and cut short. The edges of the wound should be approximated and everted rather than inverted.

There are various modifications of the *uninterrupted suture;* for example, the buttonhole stitch, in which the needle is passed over the suture after piercing the skin. It is more rapidly done than the interrupted, since only two knots are required, one at each end.

More rapid still is the *continuous suture.* After placing and tying the first stitch the two edges of the wound are whipped over and over. The disadvantage is that it does not secure accurate coaptation of the skin edges, nor does it permit the removal of one loop in case of tension or necessity for local drainage.

A method has been devised of closing wounds by means of a clamp called the *Michel clamp.* This is a small strip of metal similar to a clip to hold papers. By means of a special pair of forceps these are applied to the margins of the wound and pressed together. They are removed by another special instrument which is inserted into rings in the side of the clamp, and by closing the jaws spreads the ends of the clamp apart.

In vascular situations where the wound is cleanly incised the *subcuticular stitch* will give the smallest possible scar, but it has the disadvantage of not allowing the exit of wound secretions. The needle is entered some distance from the edge of the wound and brought out in the skin near the end of the wound. It is then entered on the opposite side, picking up the cutis vera only and not coming to the surface. It is thus carried back and forth until the other end is reached and then passed out through the skin at some distance from the wound but in a straight line. On pulling the ends of the suture tight the wound is perfectly closed. It is often best to place at the end of the wound a small strip of rubber or gutta-percha tissue to the depths of the wound for twenty-four hours. Silkworm-gut, silver or bronze wire, are usually employed, but require removal; catgut may be used and does not require removal. This suture is only applicable to straight incised wounds.

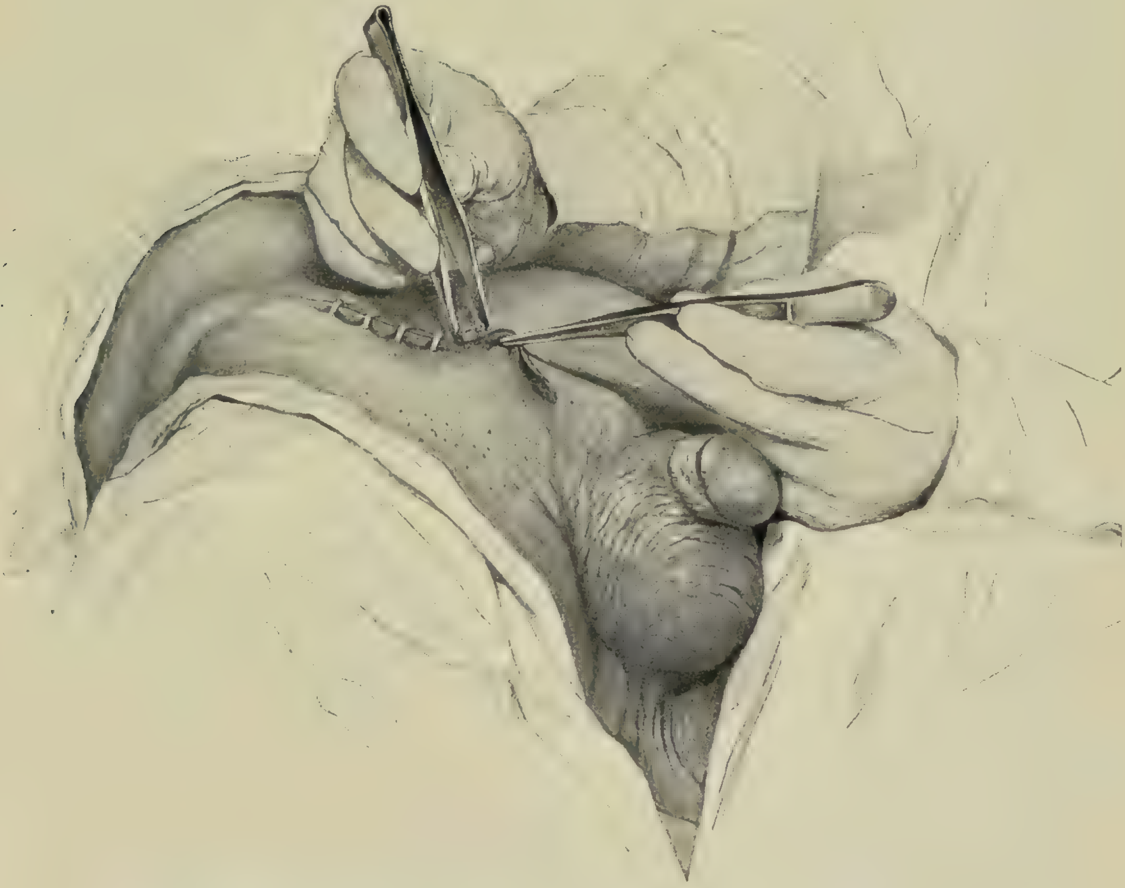


FIG 247.—METHOD OF APPLYING THE MICHEL CLAMP (Zuckerkandl).

Still another method of closing wounds with a minimum of scar is that of employing a very small needle, introducing interrupted or continuous stitches of horsehair or of extremely fine silkworm-gut, or a piece of untwisted 00 silk, then removing them in twenty-four hours and applying silver collodion dressing. This consists in applying a piece of silver foil directly upon the wound, over which collodion is applied.

Closure by the occlusion method by the *use of collodion* is not usually successful because of the retention of wound secretion. In large gaping wounds when the conditions present are favorable for complete closure, partial closure by interrupted stitches at wide intervals, inserted at a distance from the margin, including the deeper tissues and tied so lightly as barely to approximate the skin is often satisfactory.

In wounds near the flexor surfaces of joints the *fixation of the limb* may in itself effect a good closure. The use of adhesive plaster directly upon the wound surface is mentioned only to be condemned. Adhesive plaster is permissible only when gauze or other absorptive material is placed next the wound to assure free discharge, the plaster approximating the side of the wound for a distance. Wounds may also be approximated by adhesive plasters as follows: A strip of plaster longer than the wound is pressed upon the skin parallel to the wound a short distance from its margin, then these are connected by cross strips or stitches drawing together the wound margins.

In suitable cases one of the most valuable and efficient methods of wound closure is by skilful bandaging with a wet gauze roller.

There is one general caution of the greatest importance which should apply to every case, that is, *sutures must not be tied tightly*. This constitutes the most common error in the closure of wounds. Sutures tied too tightly cut, constrict, and destroy contiguous tissues during the swelling that follows. They retain wound secretion, lower the resistance, increase infection, and cause unnecessary pain. One of the valuable properties of horsehair is its elasticity, whereby it may accommodate itself in a certain degree to the swelling. Then, too, it can scarcely be tied tightly without breaking, thus preventing in a measure the most common error. Either plain or chromicized gut is unsuitable because of the irritation incident to its swelling. Horsehair, silkworm-gut, and fine silk are at present probably most desirable.

Dressings.—As a rule, occlusive dressings should not be used. In traumatic surgery one of the most satisfactory dressings for general purposes is a 1 : 10,000 moist bichlorid dressing. According to the urgency, the dressings may be moistened by removing the outer bandages and applying the warm solution from every four hours to once daily. On account of the irritation such dressing must be used with caution on the face and neck, and other sensitive tissue, likewise in children. In these instances a boric acid solution may be substituted. When dry dressings are used, either plain gauze, or iodoform gauze with or without silver foil upon the wound, are most generally useful. In the case of toy pistol or other wounds in which the possibility of tetanus infection exists, wounds should be dressed very lightly with dry gauze, giving free circulation of oxygen, to kill, if possible, the anaërobic bacilli. Dressings should be voluminous, carefully adjusted, and loosely applied.

Rest.—In planning the treatment of wounds the most careful consideration for the securing of physiologic rest should be made. If at or near a joint, the parts both above and below should be immobilized. In whatever part of the body, physiologic rest should as nearly as possible be secured. If the wound be of the hand or the wrist, a comfortable splint should be applied; if of the foot or leg, the patient should be in the recumbent posture with the part in the position of elevation. The factor of rest, next to that of cleansing and dressing, is most important. Physiologic rest means not only less pain, less reaction, but a more rapid and certain repair.

Under ordinary circumstances no special constitutional treatment is necessary beyond that of securing good hygienic surroundings, easily digested diet, restricted at first, and free action of the bowels. If there is great pain, opiates may become necessary; but here, as in other surgical indications for anodynes, a minimum amount only should be given. Usually rest and elevation and relief of tension will be of greater benefit than opiates. If there is great restlessness, a bromid may suffice; if marked insomnia, one of the ordinary hypnotics. Great restlessness with excitement and occasional delirium, without special evidence of pain or infective process, must call attention to the possible development of delirium tremens, for a relatively slight injury, such as a crushed toe or a simple fracture, may precipitate an attack in one who has been a steady though perhaps not an excessive drinker. In such cases, in addition to the ordinary therapeutic remedies, the regular administration of whisky should be advised.

BRUSH BURNS.

A brush burn is produced by contact of the body with a rapidly moving object, such as a rope or belt of machinery. The injury is caused both by wearing away of tissues, as by a grindstone, and by the heat generated by friction. In extent a brush burn may vary from a superficial abrasion to an extensive loss of integument and subcutaneous tissues. The pain is usually intense on account of the large area of skin involved. From the nature of the wound no closure is possible. The raw and oozing surface should be washed with a mild antiseptic and protected by a large antiseptic absorbent dressing, since the serous discharge is very large. Care must be taken not to use too large a quantity of a strong antiseptic on account of the danger of constitutional symptoms from absorption. Cases of carbolic acid poisoning have occurred from using carbolized vaselin on large raw surfaces. The cases should be handled in the same manner as burns from other causes, by skin-grafting by the Thiersch method, care being taken to prevent subsequent deformity from contact of scar tissue.

INCISED WOUNDS.

An incised wound is one which is clean cut by a sharp instrument so that a very small portion of the neighboring tissue is devitalized. If such a wound is quickly made, pain may be very slight at first, to be followed later by burning pain. Hemorrhage is usually considerable and may be rapidly fatal if large arteries are involved, because cleanly cut vessels always bleed more than torn or crushed vessels. Shock is usually not great unless the wounds are extensive and associated with considerable hemorrhage.

The first point in the treatment is to stop the bleeding, then search for damaged structures in the depths. If nerves or tendons are cut, suture them at once. It must be remembered that the proximal end of a tendon may retract and be difficult to find. Enlarge the wound if necessary to perform the suture properly. Divided muscles should also be sutured. The wound should be closed by one of the methods above described, with or without drainage as the necessity of the case demands.

CONTUSED WOUNDS.

Contused wounds are open wounds in which the edges are contused. They are produced by blunt objects striking the body, such as blows from a club. The chief factor which distinguishes a contused wound from an incised wound is the condition of the margins. The blunt force crushes and devitalizes the tissues along the edges of the wound. In addition to the damage done by the blow itself, the outpouring of blood and lymph in the margins, where it cannot escape, still further devitalizes the tissues by constant pressure and interference with circulation and nutrition. There is, therefore, a zone, narrow or wide, depending upon the amount of contusion, which becomes necrotic and must either be carried off by absorption, by fatty degeneration, or by sloughing off into the wound. The pain of a contused wound is greater than that of an incised wound of equal depth and extent, owing to the bruising, crushing, and subsequent pressure by hemorrhage or exudate on a very large number of the fine nerve terminations in the skin. The greater the contusing, the greater the number of nerve-endings injured and the greater the pain. The hemorrhage is usually not considerable unless large vessels are torn, since bruised vessels, for the reason already stated, do not tend to bleed. The swelling and discoloration are considerable owing to the extravasation of blood and lymph into the tissues, from which they cannot escape through the breach in the skin.

Treatment.—The aim of the surgeon in all cases of wounds is to obtain union by first intention wherever possible. In wounds where the contusion is but slight and proper cleansing can be carried out, a contused wound may be sutured without drainage, but the stitches must be few, far apart, and loosely tied. In the majority of cases where the contusion is at all extensive the wound should be packed open with gauze and allowed to granulate; or, at most, one or two loose sutures applied to a portion of the wound and the rest drained. The importance of position as an aid in keeping the wound edges in apposition, and of rest in accelerating the healing, must not be overlooked.

LACERATED WOUNDS.

A lacerated wound is an open wound in which there is tearing or crushing of the tissues, making the margins irregular and ragged. Wounds of this class are most commonly made by the teeth or claws of animals or by certain kinds of machinery. In a lacerated wound the same characteristics obtain as in a contused wound but to a greater extent. The breach in the skin and underlying tissues is more irregular and the contusion of the margins greater. The severity of this class of wounds extends from small tears by a nail, for example, to extensive crushes by cars or heavy machinery. The amount of damage to the tissues adjoining the wound depends chiefly upon the sharpness of the instrument which inflicts the injury, but also upon the speed of the object. For example, it has been found that in lacerations produced by slowly moving railroad trains the devitalization of the tissues is a minimum, while in those made by fast trains it is much greater, so that while it is safe to amputate near the margin of a crush from a slow train, in injuries from a fast train a wider margin must be removed to avoid subsequent gangrene of the stump.

The pain of wounds at the time of their occurrence depends on many bodily and emotional conditions, as has been stated elsewhere, but, as a rule, the pain is least in incised wounds, greater in contused, and greatest in lacerated wounds until the state of profound shock occurs which completely blunts the sensorium.

Shock (considered in detail elsewhere) follows the same rule as pain: least in incised, greatest in lacerated and contused wounds.

Hemorrhage is least in lacerated wounds. It is not uncommon to see extensive lacerated wounds or mangled limbs with very little bleeding The swelling in and about a lacerated wound is great, and when the wound is packed open the discharge of serum is very large.

Treatment.—In the treatment of lacerated wounds the condition of shock is of great importance and must receive the first attention. The element of pain in producing and prolonging this condition is also very important. In an extensive laceration, such as the crush of a limb which has produced extensive mangling and great shock, the greatest care and judgment should be used in deciding whether the patient can stand the additional shock of an operation or whether the irritation of a mangled limb will be the less detrimental. One of the greatest advances in modern surgery has been the method of preventing shock by blocking the nerve-trunks with cocain. By this method a mangled limb may be removed without materially increasing shock and the condition of the patient improved by removal of this cause of irritation and pain. A lacerated wound can never be safely closed. After as careful cleansing as is compatible with the patient's general condition the wound should be packed open with gauze and allowed to granulate, or, at least, if the gaping be very wide, one or two stay stitches introduced. In suitable cases a lacerated or contused wound may be converted into an incised wound by cutting away the margins, and may then be closed as any incised wound.

AVULSION OF LIMBS.

Up to within a comparatively recent period the avulsion of a limb was supposed to be always fatal. By modern treatment, however, a few of the cases have been saved. The following is the history of such a case. The sleeve of a shop-girl was caught in a revolving shaft, causing avulsion of the arm at the shoulder-joint. The end of the brachial artery projected among the torn tissues. There was little hemorrhage. The large nerve-trunks were cocainized, the wound cleaned up by cutting off the ragged tags of tissue and sponging off with an antiseptic. The profound shock was met by elastic bandaging of the lower extremities and the abdomen and by saline infusion.

The injury usually occurs by the extremity being caught in the belt of machinery, or by a moving train. The member is torn off at a joint; the muscle bellies are torn through rather than the tendinous extremities; the nerves are frequently ruptured at a distance from the wound, so that either the stumps of the nerves are deeply buried in the sound structures above, or are torn within the avulsed limb and hang exposed for several inches from the trunk. The hemorrhage is very slight, owing to the tearing of the vessels. In the case of avulsion of an arm, for example, the torn end of the brachial artery may frequently be seen projecting from the wound and rising and falling with the rise and fall of the blood-pressure or each heart-beat, like the coiled spring in a steam-gage.

The chief cause of death is shock. With the modern knowledge of this condition and its treatment the outlook in these cases is better than formerly. The shock should be carefully treated. If the large nerve-trunks are dangling from the wound, they may be carefully infiltrated with cocain, as high as possible, and the exposed part removed. A ligature should be placed about the main vessel. But little attempt should be made to trim up the ragged edges or to cleanse the wound thoroughly. A large moist antiseptic dressing should be applied and the patient's general condition treated.

AVULSION OF THE SCALP.

This occurs almost exclusively in girls working in factories, whose long hair becomes caught in revolving machinery. The tissues of the scalp covering the bones of the skull are arranged in five layers —the skin, the subcutaneous fat, the epicranial aponeurosis, a layer of loose areolar tissue, and the pericranium. The skin and epicranial aponeurosis are closely bound together by numerous bands of fibrous tissue so that movements of the occipitofrontalis muscle move the integument. The areolar tissue between the aponeurosis and the pericranium is loose and without fat. From these anatomic conditions, when the skin of the scalp is torn off the plane of separation is in the areolar tissue between the aponeurosis and the pericranium. Very commonly, however, portions of the pericranium are also torn away, leaving the bones of the skull bare. The loss of substance may be very extensive. A case[2] is reported in which the entire scalp, together with all the left ear except the tragus, the antitragus, the lobule and all of the integument and subcutaneous tissue down to the fifth cervical spine behind and the zygoma and bridge of the nose in front, including about half the left and portion of the right eyelid, were torn off by a belt. The patient recovered, the defects being supplied by Thiersch grafts. The shock varies and may be slight. The hemorrhage is inconsiderable.

The principle of treating such cases is by skin grafting. If shock is present, it is best to apply a moist antiseptic dressing for twenty-four to forty-eight hours and then apply Thiersch grafts, or the grafting may be delayed longer until the wound begins to granulate. Grafts may be placed directly on the bare bone with occasional success, but, as a rule, there is necrosis and exfoliation of a thin scale of bone from the external table. Granulations first spring up through the sutures between the bones, later granulations start within the bones and by their growth elevate a very thin plate. This scale is easily removed, leaving healthy granulations which form a good surface for grafting.

In a patient examined recently two years after injury, the wound, an area of six by eight inches, was covered by a thin but soft and pliable skin. This skin was freely movable over the skull except in places where the bones of the skull were bared, where the skin was but very slightly movable. The area was not sensitive and caused merely a feeling of discomfort, as if water were being poured over the head, on changes in the weather. Patients who have suffered an avulsion of a portion of the scalp can conceal the deformity very well with a wig.

PUNCTURED WOUNDS.

A punctured wound is one in which there is but slight opening in the integument with comparatively great depth of penetration. This class includes gunshot and stab wounds, and wounds made by slender pointed objects, as nails or needles. The amount of injury done in the depth of the wound is not apparent. Important organs or large vessels may be injured. The diagnosis of such injuries must be made by objective and subjective symptoms other than those of the wound of the skin. Evidence of internal hemorrhage or of interference with the circulation in the extremities or the existence of a hematoma must be sought for, indicating injury to great vessels. Paralysis and nervous disturbance must be looked for. The urine must be examined for the blood if there is any suspicion of injury to the urinary tract. The most difficult cases are punctured wounds of the abdomen. There is one invariable rule in all punctured wounds of the abdominal wall in which there is the slightest possibility that the instrument has penetrated the peritoneal cavity: operate as soon as possible, and with the aseptic precautions and assistants required for an operation on the abdominal viscera. The wound in the skin should be incised and the tract of the wound traced carefully through each layer of the wall. If the peritoneal cavity has not been opened by the wound, it need not be by the operation. If the cavity is not entered no harm is done, while if a wounded viscus is found the patient may be saved from what would have been almost certain death from hemorrhage or sepsis.

Do not probe a punctured wound. Much more harm than good has been caused by injudicious probing. But little information of value can be obtained by this means and oftentimes infection is carried from the surface into an otherwise aseptic wound. If a foreign body requiring removal is in the depths of the wound it is better to lay the wound freely open.

The second great danger of punctured wounds is the liability of the introduction of foreign material, especially tetanus bacilli. This organism is very widely disseminated and finds its natural habitat in the soil, especially about gardens and barn-yards. These bacteria, being anaërobic, flourish in the depths of punctured wounds from which air is excluded. But very few of the organisms are sufficient to cause fatal tetanus, and on account of lack of local signs, there is no way of determining whether a wound is infected or not. All punctured wounds, therefore, should be treated as if bacilli were present.

The **symptoms** of punctured wounds are very variable, but the importance of the immediate symptoms of the wound itself are overshadowed by the presence or absence of symptoms arising from damage to other important organs. Punctured wounds by blank cartridges need especial mention. Every year following Fourth of July celebrations there have been many deaths from tetanus from injuries by cartridge wads. Tetanus bacilli have been demonstrated in wads taken from cartridges bought in the open market.[3] These bacilli when introduced into the depths of a punctured wound have an ideal place to proliferate. They are lodged in damaged tissue, the resistance of which is lowered, and are protected from oxygen. The treatment of these wounds has been thoroughly studied by Dudley P. Allen in his clinic at Lakeside Hospital. According to his experience, these wounds should be thoroughly opened under full surgical anesthesia, all bits of wad or powder removed, the wound flushed out with an antiseptic, and lightly packed open with iodoform gauze. Another class of punctured wounds in which the danger of tetanus is great is wounds of the foot by nails or garden implements, since the soil is the natural habitat of the tetanus bacilli. Such wounds should be treated in a manner similar to blank cartridge wounds. The methods of combating tetanus by serum, etc., are elsewhere discussed.

Another condition exists in punctured wounds which makes them especially dangerous in cases of infection. Where the implement pierces muscle or several muscular planes the depth of the wound is often shut off from the skin wound by the contraction of the muscle or the relaxation of the previously contracted muscle. If infection is introduced below these muscular planes, the pus cannot find exit and frequently burrows extensively below the fascia without appearing at the surface. The diagnosis consists in finding evidence of deep, undrained infection. The treatment is in accordance with the general surgical principle to open freely and pack the abscess cavity if present, or drain a diffuse cellulitis.

GUNSHOT WOUNDS.

The effect of a gunshot wound is dependent largely upon the tissues and organs involved, whether hollow viscera, brain, blood-vessels, nerve-trunks, etc., the nature of the bullet, whether of lead or steel, large or small, the velocity, the physical state of the patient, and the immediate after-care. (For full consideration of gunshot wounds, and in particular regions, see Military Surgery.)

Tissues or Organs.—As to their immediate effects, gunshot wounds of the brain, especially in regions of the base, the upper portions of the spinal cord, the heart, and the great blood-vessels, are most important, as they are likely to cause immediate death. Wounds of the hollow viscera, lungs, kidneys, and large joints, do not, as a rule, cause immediate death, but they are exceedingly grave, whereas wounds involving the skin, fascia, muscles, tendons, and other soft tissues under ordinary circumstances are not dangerous.

The immediate effect of a gunshot wound involving the brain depends primarily upon the region involved. Wounds through the frontal, parietal, or temporal lobes may cause only temporary changes in the circulation and respiration, and later cause death by infection or hemorrhage. Wounds through the base, causing disruption of the centers in the medulla either by direct solution of continuity or by complete functional dissolution from concussion, are most fatal. It is well to bear in mind the researches of Horsley,[4] that the most striking immediate effect of gunshot wounds involving the brain is the cessation of respiration. The blood-pressure itself may even be undisturbed while the respirations are totally inhibited. In offering immediate aid in such cases, artificial respiration demands first consideration. Gunshot wounds of the lower posterior aspect of the skull without penetration may, by the functional disruption of the centers in the medulla due to the concussion, cause instant death. The same may be true of wounds of the neck near the skull, involving the vertebra but not doing physical damage to the cord. Then, too, wounds merely touching the skin or passing through the soft parts without contact with large vessels or important nerves may cause momentary inhibition of respiration and of the circulation and inhibit the passage of motor impulses, thus causing the subject to drop to the ground, though death generally does not immediately occur.

In capturing wild horses use is made of this phenomena in the so-called "grazing," which consists in firing a bullet so as to come merely in contact with the neck near the head, knocking down the horse preparatory to capture.

In the Spanish-American War an instance of this kind in man came under my observation. A captain of infantry while charging up a hill suddenly fell to the ground, and for a moment was unconscious. He then arose, felt a little dizzy, and was surprised to find blood trickling down his neck. Seeing him perhaps twenty minutes later, I found the entrance and exit marks of a Mauser bullet whose course lay wholly in the tissues of the skin, fascia, and muscles of the back of the neck over the third vertebra.

Wounds of the spinal cord below the cervical region virtually never cause immediate death, though the termination is frequently fatal from the complications arising from paralysis. The principal of these are cystitis with ascending infection of the kidneys, infection and exhaustion from extensive bedsores, etc.

Wounds involving the face and mouth unless complicated are usually followed by recovery. In wounds of the neck the gravity is dependent entirely upon the structures involved. Immediate death may follow the division of large vessels, later death from pneumonia if the trachea, the superior laryngeals, or both hypoglossals are involved.

The gravity of gunshot wounds of the thorax is dependent almost wholly upon the part involved. If the heart or great blood-vessels are penetrated immediate death usually follows. Among the well-known exceptions are those in which the ventricles of the heart only are penetrated. The later risks are those of pulmonary hemorrhage, pneumonia, aneurism, empyema, chylothorax, and starvation if the thoracic duct be involved.

In the abdomen, as in the thorax, the prognosis depends wholly upon the track of the bullet. Perforation of the stomach or intestines, or of the bladder, on account of infection is extremely grave. Penetration of the liver and spleen, on account of the hemorrhage; of the pancreas on account of the hemorrhage and the effect of the pancreatic juices upon the intraperitoneal tissues, are important. Gunshot wounds of large joints are grave on account of the danger of infection.

The Composition of the Bullet.—Bullets made of soft metal, such as lead or other compounds whose physical properties permit mushrooming on impaction with solid tissue, such as bone, as in the dum-dum bullets, cause more laceration and contusion, penetrate less deeply, and lodge more frequently, causing the greatest damage. The effect of such bullets is so mutilating as to be forbidden by the rules of war among civilized nations. The modern army rifle bullet, steel-jacketed, slender, and long, does not ordinarily mushroom, finds less resistance in tissue, penetrates more deeply, lodges less frequently, and causes decidedly less damage.

In civil practice the ordinary leaden revolver bullet is one of the most common causes of penetrating wounds. Not only do these bullets mushroom, lacerate, contuse, and lodge, but pieces are often detached and lodged at a distance from the remaining mass of the bullet.

Velocity.—The greatest damage is probably inflicted at close range with high initial velocity, and under these circumstances shattering is much more marked. The minimum shattering is found in the medium velocity, while a well-spent ball causes a little more. The effect of modern arms has been well studied by Major Lagarde, Nancrede, and others.

Physical State of the Patient. — Patients in a low physical or mental state, such as suicides in lingering incurable diseases, soldiers fatigued by long marches and reduced by starvation or cold, by fear and defeat, by homesickness, or drunken debauchees, or in any state of general health which would from an operative standpoint be considered bad risks, are peculiarly susceptible to the effects of such wounds.

Immediate After-care.—There is probably no other factor, except in those causing immediate death, which is so important in determining the result of gunshot wounds as the immediate care. With respect to this the prevention of infection is of paramount importance. The arrest of hemorrhage is a surgical axiom, but the prevention of infection still needs to be emphasized. All gunshot wounds in civil life may be presumed to be infected at the point of entrance and the point of exit. The inner tract may be presumed to be sterile, or, if not, the tissues usually overcome the infection. Based on both theoretic and practical grounds, probing should never be done so long as the entrance or exit wounds have not been sterilized. The probe undoubtedly has been responsible for more harm than good in the treatment of gunshot wounds. The probe would better be entirely omitted from the armamentarium of all but experienced men whose surgical training has been so thorough as not to permit them to probe a bullet wound except the wound and whole operative field be prepared as carefully as for the entrance into the clean peritoneal cavity. The temporary care and dressing on the field or at the place of accident in the majority of instances is the determining factor governing the result.

The gunshot wounds of civil life, as before stated, are mainly inflicted by the heavy, leaden revolver bullet at close range in saloon brawls, or by suicides, and constitute a very unfavorable group of cases.

Treatment.—Uncomplicated gunshot wounds of the extremities, of the walls of the abdomen, of the thorax, of the back, of the neck, and of the scalp, are best treated by immediate cleansing of the open wound and the application of moist antiseptic dressings. Even when joints are penetrated, in the majority of instances it would be better to guard first against infection and wait for further indication for treatment. The present accurate method of locating bullets by means of the x-ray has given modern surgery a tremendous advantage in avoiding the troublesome and often disappointing search for the bullet. It is now well known that bullets may remain for an indefinite period in the tissues without producing any harm. The excision of the bullet, as a rule, is of little importance compared with the urgent need of the prevention of infection. In penetrating wounds of the abdomen in civil life practical experience and experimental research have shown that the lead bullet is so certain of doing serious damage that the expectant plan here should not hold, and the rule should be rigid for immediate operative exploration, not with the primary object of finding the bullet, but of repairing the damage and preventing complications. In the extremities the tendency is to drop the operative course and direct attention only to the prevention of infection. Whenever at all permissible, direct penetrating wounds of the abdomen should be immediately explored, and should the bullet happily have missed penetrating a viscus or causing hemorrhage, but little harm will be done; on the other hand, the almost certain perforation or hemorrhage is, under the expectant plan of treatment, extremely liable to ultimately cause death. In wounds of the thorax, on the contrary, the rule applied to the extremities should prevail, and operative measures should be withheld until such symptoms as hemorrhage, or infection, or certain lesion of the heart have been established. If nerve-trunks have been severed they should be immediately reunited. If the bullet involves the spinal cord or is lodged within it, immediate extraction should be done. The exact position of the bullet in such cases can be so accurately determined by means of the x-ray that in the case of the spinal cord the obvious symptoms of paralysis, of increased reflexes, etc., together with the x-ray, make out so clear an indication that it need not any longer be considered in the light of an exploration.

In penetrating wounds of the skull, as in those of the chest, one should take every measure to prevent infection and wait for symptoms to determine what further measures should be employed. In these instances, however, certain exceptions must be made. The prevention of infection might be accomplished by the care of the surface wound, but in penetrations of the skull spicula of bone, hair, etc., are almost certain to be driven in, and every case on this ground, as in every case of compound comminuted fracture of the skull, should at once be explored, the opening in the skull amplified, and fragments of bone, etc., removed under the most rigid precautions. Under certain exceptional cases the ball may be accurately located by the x-ray and removed according to the method of Sweet.

STAB WOUNDS.

Stab wounds are punctured wounds made by the more or less sharp blade of a knife, dirk, or similar instruments. They do not differ in any marked particular from punctured wounds in general except that great vessels and nerves are more apt to be severed than in wounds by blunter objects.

Stab wounds may occur in any part of the body, even the brain is not exempt. Keen reports two cases in which the skull had been pierced by the blade of a pocket-knife and the blade broken off within. Such wounds require immediate exploration, but with all aseptic precautions.

Stab wounds of the neck may involve the great vessels and may lead to rapidly fatal hemorrhage, or may wound artery and vein and give rise later to arteriovenous aneurism.

In the chest the knife may perforate the lungs or heart. A wounded lung may cause subcutaneous emphysema, a pneumothorax, or hemothorax. Emphysema, as a rule, disappears spontaneously, but if it threatens life or causes suppuration, multiple incisions should be made. In cases of pneumothorax where the air enters through the external wound, apply a piece of rubber dam over the wound. This will allow air in the pleural cavity to be expelled during expiration, but by its valve-like action will not allow it to return. If the pneumothorax threatens life, aspirate the air.

Hemorrhage from an intercostal artery can be controlled by thrusting the center of a piece of gauze into the pleural cavity, after the manner of the finger of a glove, and packing into it a long strip of gauze to form a ball at the tip; then by pulling the gauze outward the artery may be compressed against the rib. The artery, being concealed by the rib, is difficult to tie, but by stripping the periosteum from the lower edge of the rib and including it in the ligature the bleeding may be controlled. Hemorrhage from the lung is more difficult to control, but unless large vessels are injured will cease spontaneously as the lung collapses.

Stab wounds of the heart are not always immediately fatal, some cases having survived many hours. A number of cases are on record in which the pericardium has been opened and the heart itself sutured.

Great emphasis must be placed on the necessity of the exploration of all stab wounds of the abdomen. A woman was stabbed in the epigastric region, to the right of the median line, with a penknife. The wound in the skin was excised and a similar wound found in the anterior sheath of the rectus. This was enlarged and the tract of the knife followed through the muscle and posterior sheath of the rectus, but the peritoneum was found intact. The peritoneal cavity was not opened. The wound was sutured and healed by first intention.

A second case is that of a laborer. He was stabbed below the umbilicus with a pocket-knife. Twenty-four hours later the wound was followed down in a similar manner. The peritoneum was found pierced. A laparotomy was done and the intestines searched for injury. A cut half an inch long was found in the ileum and sutured, but the man succumbed to peritoneal infection. If this puncture of the intestine had been immediately closed, his life might have been saved. Stab wounds of special regions will be considered in their proper sections. In general, it may be said that in all uncomplicated stab wounds it is best not to close on account of the danger of infection, but to insert a drain, enlarging the opening in the skin if necessary.

WOUNDS OF MUCOUS MEMBRANES.

The mucous membranes which are the most exposed to accidental wounds are those of the nasal and buccal cavities. Any mucous membrane, however, such as that of the urethra, the intestinal tract, the rectum, or the vagina, may be subjected to operation wounds and also to accidental wounds in certain instances, but in accidental wounds of the urethra and intestinal canal, especially, the wound in the mucous membrane is overshadowed in importance by other elements, such as the extravasation of urine or the infection of the peritoneal cavity. There are two characteristics in which wounds of the mucous membrane differ from wounds of the skin. First, they are always infected; the mouth, nose, intestinal canal, urethra, and vagina are the natural habitat of numerous forms of bacteria. These bacteria, it is true, are largely nonpathogenic; in the intestines, for example, chiefly putrefactive, but nevertheless pyogenic bacteria are almost invariably present, and often in very virulent forms; even after careful cleansing of the mucous membrane previous to operation the surface is not sterile. The second characteristic is the kindly way in which wounds of the mucous membrane heal. Serious infections do occur in these wounds, but they are very rare.

Wounds of the Buccal Cavity.—Incised wounds of the mouth and tongue are usually made by some sharp instrument, such as a knife or a bit of foreign material in the food, as a piece of glass. Wounds made by the teeth, as by biting the tongue in an epileptic fit, or by blows, forcing the lip or cheek against the teeth, are always more or less contused or even lacerated. A punctured wound may be made by a fish-bone or the tine of a fork. The tongue and mouth are very vascular and considerable hemorrhage may take place. As a rule, the bleeding ceases spontaneously; if it does not, the pressure of a gauze pad against the wound will usually be sufficient. In rare instances a large blood-vessel may be divided. The large artery, a branch of the external carotid to the tonsil, may cause considerable hemorrhage after tonsillotomy. The lingual artery in the tongue is also of considerable size and may give rise to troublesome hemorrhage. In case these large vessels cannot be exposed and tied in the wound, the external carotid artery should be ligated in the neck.

The first step in the treatment of wounds of the mouth is to check the hemorrhage. The next factor of importance is to limit the infection as much as possible. It is impossible to secure absolute asepsis in the buccal cavity. Carious teeth, which are the breeding-places of countless bacteria, should be removed and the teeth cleansed with a stiff brush and the gums thoroughly rubbed with a cotton swab saturated with a mild antiseptic or even physiologic salt solution, and the entire mouth rinsed out with a wash, such as hydrogen peroxid or tincture of myrrh. Small wounds need no suture. Large incised or lacerated wounds should be caught together with interrupted sutures, preferably of absorbable material, as catgut. Silk, horsehair, or fine silkworm-gut may be used, but cause unnecessary pain in the removal of the stitches. In lacerated wounds no part of the ragged edge should be removed, as a considerable laceration will heal well in such a vascular situation. In wounds of the lip, extending into the surrounding skin, great care must be taken to secure accurate coaptation of the red margin of the lip, or considerable disfigurement will result. The stitches must be few and far apart and loosely tied to allow for drainage between them and for the subsequent swelling due to infection. It is necessary to insert an artificial drain only in very large and extensive lacerations. The after-treatment consists in the care of the teeth and a cleansing mouth-wash.

Wounds of the Nasal Cavity.—Wounds of the nasal mucous membrane are usually produced by some cutting instrument or by rupture from a blow on the nose, or occasionally by a sharp spicula of bone in fracture of the nose. The mucous membrane of the nose is very richly supplied with blood-vessels superficially placed, owing to the function of the nose to warm and moisten the inspired air. Considerable hemorrhage takes place, therefore, in wounds of the nose. The point from which the greatest bleeding comes is the septum. Cold, pressure from without, or an astringent spray, such as antipyrin, 5 to 10 per cent. solution, or adrenalin, 1 : 1000, is usually sufficient to stop the hemorrhage. In severe cases, however, it may be necessary to pack the entire nasal cavity through the nostrils.

In packing the posterior nares, pass a Bellocq's canula, threaded with a piece of strong silk, through the side of the nose to be packed; when the tip appears in the mouth below the soft palate, seize the silk with a pair of forceps and withdraw it through the mouth, then remove the canula. This gives a silk thread entering the nose and returning through the mouth. To the middle of this thread tie a ball of absorbent cotton somewhat larger than the last joint of the thumb; draw on the thread in the nose and guide the cotton with the finger around the palate until it is firmly impacted in the posterior nares. Leave the thread projecting from the mouth so that the plug can be easily removed, and tie the nasal end about another ball of cotton which will serve as an anterior plug. In place of the special canula a gum-elastic or soft-rubber catheter may be used, tying the silk to the tip. The cavity is then packed through the nares by crowding in cotton until the bleeding is controlled. The plug in the posterior nares should not be allowed to remain longer than twenty-four hours, on account of the ease with which it becomes infected in this situation and endangers the middle ear through the Eustachian tube. If required to be continued long, it should be renewed. The use of such styptics as subsulphate of iron cannot be too strongly condemned, not only as unsurgical, but as unsafe and dangerous.

Eliot Alden reported the case of a football player whose nose was broken and the mucous membrane torn by a spicula of bone, in which it was necessary to keep the nose tightly packed for an entire week. Suture is impossible, of course, in wounds inside the nose. The treatment consists in spraying or douching the cavity with Seiler's or Dobell's solution or any mild alkaline antiseptic wash. Artificial drainage is rarely if ever indicated.

Wounds of the Urethra.—This subject will be treated in another section; mention may be made, however, of the rapidity with which defects in the mucous membrane of the urethra are repaired. A considerable gap, such as may be made by a rupture of the urethra, will be rapidly renewed by proliferation from the sound margins of the membrane.

Wounds of the Vagina.—The lining of the vagina is not a true mucous membrane, but it partakes of the same characteristics in that it is always infected but heals kindly and rapidly repairs defects.

Wounds of the Intestinal Mucous Membrane.—There is one characteristic of wounds of the hollow viscera to be mentioned here. The mucosa of the alimentary tract is not elastic while it is contained within organs with thin muscular walls. Consequently, when a hollow viscus is wounded, as by a gunshot wound, the muscular coat contracts and gapes while the mucous membrane is unable to do so. There results, therefore, a pouting of the mucosa through the wound in the muscular coat. Such a wound, with mucous surface opposed to mucous surface, cannot heal in the manner of wounds of non-mucous surfaces, by direct repair, but only by attachment to some neighboring tissue which will serve as a patch to the entire wounded area. This illustrates the necessity of operation in all cases of wounds of the hollow abdominal viscera.

INFECTED WOUNDS.

An infected wound is one in which pyogenic organisms are present and multiplying. The wound may be infected by the instrument producing it, or later by injudicious probing, or the lack of surgical cleanliness in dressings. The constitutional symptoms, fever, malaise, possibly chills, etc., are caused by the absorption of poisonous products elaborated by the bacteria themselves or produced by their action upon tissue cells. Later the bacteria may gain access to the general circulation and cause bacteriemia, or if associated with a detached portion of a thrombus pyemia may result. The local symptoms and course of the infection vary with the organism present. The symptoms common to all infected wounds are the classic ones of inflammation, pain, redness, heat, and swelling.

Staphylococcus infections show little tendency to spread and are characterized by the formation of considerable pus. The discharge from the wound is at first thin and watery, but later, as a defensive wall of granulation is thrown around the seat of infection, the pus becomes of a creamy appearance. This is the "laudable pus" of pre-antiseptic days, and is well named, for if pus be present, this form is least dangerous, showing as it does an active resistance of the tissues against the infective organism.

Streptococcus infections are more serious and rapid in their progress. There is not such a tendency to pus formation, but the edema is greater and the organism travels more rapidly along the lymph-channels to the nearest seat of lymph nodes, forming painful red lines along the course of the lymphatic vessels. This organism if not checked tends to enter the general circulation.

Treatment.—The first surgical principle in the treatment of infected wounds is to afford free drainage, making it easier for the organisms and their products to pass outward rather than inward. If the wound has been closed, remove the stitches, cleanse with an antiseptic, and pack with iodoform gauze. Apply over the wound a large dressing saturated with a hot solution of a mild antiseptic and cover with an impervious material, such as oiled silk. The outer dressings should be frequently removed and the part soaked or bathed in a hot, weak antiseptic, and the dressings reapplied as before. There is nothing gained by removing the old packing and applying fresh, for the new gauze will in a very few minutes be as saturated with pus as the former gauze and the patient will have been caused unnecessary pain.

If the patient is progressing satisfactorily, as shown by a lowering of the temperature and a diminution of the redness, pain, and swelling of the wound, the original packing may be left in from five to seven days. At the end of this time the gauze can be easily and painlessly removed, since the discharge of pus from the walls of the wound will loosen it and in time float it out. If the patient is doing well the rule should be, do not remove packing until it can be done without pain. If the patient is not doing well under the original packing, it shows either faulty technic or an extension of the infection. In this case a thorough revision of the dressing must be made, under an anesthetic if necessary. The packing must be removed and a careful search made for pockets which were either overlooked before or have been formed since the former dressing. The wound should then be repacked and treated as before. After the removal of the original packing the wound will be found beginning to granulate. If many sloughs are present, they should be cut off, if it can be done without pain or bleeding, the wound irrigated, and a drain inserted.

There is a distinction between a pack and a drain. A pack fills an entire cavity, so that the gauze everywhere comes in contact with the walls and is used either to stop bleeding from the wall of a cavity or to absorb pus from every part of an infected wound. A drain, on the other hand, is a piece of gauze, rubber tubing, or other material inserted into a wound loosely to afford an outlet to the secretions, serum, or pus, as the case may be, but does not fill the entire cavity.

After an infected wound begins to granulate a drain is all that is necessary, but care must be used that the drain does not block up the entire outlet, acting as a cork in a bottle. The drain must not be allowed to remain in place too long, for it must be remembered that the drain itself keeps the wound open and keeps up the discharge of pus. It is manifestly impossible, therefore, to drain a wound until all the pus formation ceases. All gauze should be removed when the wound is granulating well and the opening in the skin is large enough to permit the exit of the discharge from below.

Another factor of importance is the outside dressing. At first it should be hot and moist, but if moisture is kept in contact with the skin for too long a time the skin becomes white and macerated and is liable to be rubbed off and excoriated. After the first few days the moist dressings should be changed to dry, and after each bathing of the part it should be carefully dried and dry sterile gauze applied. The constitutional treatment consists in as liberal a diet as the inactivity of the patient permits, and free catharsis.

The treatment of diphtheria with antitoxin has been so extraordinarily successful that many efforts have been made to secure an antistreptococcic serum for use in streptococcus infections. Thus far only partial success has been attained. Undoubtedly there are many varieties of streptococci. The serum obtained from an animal immunized to a particular variety of streptococcus seems to have a curative effect on infections with the same variety but not on infections with other varieties. Clinically or microscopically we cannot tell which variety of organism we have present, and therefore which antiserum to use. To avoid this difficulty, manufacturers are now making what they call "polivalent" antistrepticoccic serum; that is, serum from animals which have been immunized to as many varieties of streptococci as possible, so that the chances of obtaining the proper antiserum are increased. Some of this polivalent serum is from horses immunized against forty-two strains of streptococci. Experimentally this polivalent serum is not as potent as the specific serum for the special variety involved, but in practice it is best to use the polivalent serum. The clinical results with antistreptococcic serum are very variable, but in any given case it may be of great value and should be used. The serum should be given early and in large doses. It is well to remember, too, that it is not only of no value but possibly does actual harm in staphylococcic infection.

There are other infections besides those by the ordinary pyogenic organism which may occur in wounds.

Tubercle bacilli may infect a wound, especially in those who do autopsies on tuberculous bodies. The usual result from such an infection is the anatomic wart, a papillomatous growth which remains local. Fatal tuberculosis has, however, occurred from an infection through an open wound in the above-mentioned manner. In operating upon tuberculous glands of the neck, or tuberculous kidneys, if the infectious material be spread about the operation wound, general tuberculosis or an infection of the wound surface which is very slow in healing may arise.

Syphilitic infections may occur in wounds which have come in contact with specific virus. In this manner chancres have appeared on the fingers and hands of physicians from examining syphilitic patients. On account of the infectious nature of the mucous patches in the mouth dentists' instruments may become infected, and if not thoroughly sterilized, may inoculate the disease in a subsequent patient.

Workers among raw wool and hides are subject to infection by anthrax. It takes the form of a malignant pustule and is a very fatal disease.

Erysipelas, tetanus, rabies, or actinomycosis may also infect wounds. The special infections will be discussed at length in special chapters.

DISSECTION WOUNDS.

A dissection wound is one made during the dissection of a dead body, either at a post-mortem examination or in the anatomic dissecting room. Their great danger lies in the liability to infection. The body of an individual who has died from infection with pyogenic bacteria contains many organisms; especially is this true if the infection is of the peritoneal cavity, as in puerperal fever. The virulence of these organisms has been sufficient to cause the death of one person, and they easily infect another. The conditions in the dissecting room are somewhat different. The pyogenic bacteria, and especially the streptococcus, die out in situations in which they are associated with other bacteria, so that by the time the body comes to the dissecting table the pathogenic bacteria are largely replaced by the bacteria of putrefaction. In addition to this the bodies are injected with a preservative fluid, so that the number of living organisms is very small. The products of putrefaction may cause a local poisoning of the wound but do not cause a true septic infection.

In performing a post-mortem or in anatomic dissections prophylaxis is of the greatest importance. No one should engage in these pursuits who has unprotected wounds or fissures on his hands, and care must be taken not to produce fresh wounds. The hair-follicles of the sound skin at times serve as an atrium of infection. It is advisable to use some artificial protection to the hands. Vaselin thoroughly rubbed in fills the cracks and fissures and pores of the skin and affords a certain amount of protection, but the vaselin itself must be sterile. Many cases of infection have occurred by rubbing in vaselin which contained organisms introduced into it at a previous autopsy. The best protection is afforded by impervious rubber gloves. Immediately on the receipt of a dissection wound it should be encouraged to bleed, thereby washing out to a certain extent the poisons introduced. It should then be thoroughly washed out under running water followed by an antiseptic. Cauterization is of doubtful value, as organisms may be imprisoned under the eschar and find a favorable situation for growth. The wound should be left wide open and a large antiseptic dressing applied. Punctured wounds are the most dangerous, and if made in the presence of an organism known to be virulent should be widely opened, disinfected, and packed.

GRANULATING WOUNDS.

The repair of wounds is described under Repair of Wounds (Chapter IX), but a few remarks will be made here as special points come up in the treatment of granulating wounds.

When a wound in the soft tissue is made, the capillaries and lymph spaces and vessels are laid open so that any poison, either chemical or the product of bacterial action, is readily absorbed into the system. Such a wound is liable to infection with pyogenic organisms. There is a determination of leukocytes to the parts, and these, together with the continual flow of lymph outward, make it progressively more difficult for absorption to take place. Then, too, the tissue cells are excited to a reaction, and by multiplying rapidly form a defensive wall about the wounded area. This wall acts as a barrier to all ingress but allows an outflow of lymph and leukocytes. From the defensive wall new capillary blood-vessels are thrown out in loops. It is these loops which give the granular appearance, hence the name granulating wound.

When the infection is severe the resistance of the tissues is overcome and granulations are either slow in forming or do not form at all. When, however, firm, red granulations are formed, we know that the tissue reaction has overcome the infection and the individual is progressing toward recovery. This is the sort of wound which discharges "laudable pus." If the body is recovering from an infection, an infected wound reaches this state in a variable period of time, depending upon the virulence of the organism and the reaction of the body. In a wound which has not been closed but in which there is no infection the granulations appear in about four days. A granulating wound cannot be infected by pyogenic organisms nor is there any absorption of chemical poisons laid on the surface, provided, of course, that the surface be not injured. If the surface of the granulations be wounded, the condition resembles that of a fresh wound, since the defensive wall is broken and blood- and lymph-vessels opened for absorption. There is this difference, however: in granulating wounds the tissues are actively reacting and they have the material on the ground, so to speak, for rapid repair of the breach in the wall, so that the new wound is quickly healed and the granulations appear as before.

Treatment.—The treatment of a granulating wound consists primarily in the protection of the tender granulations and keeping up conditions favorable for the epidermization of the wound. Epidermis is renewed from epidermis only. A granulating wound must therefore be covered by skin from the margins. The new cells multiply best on a level surface; they will not readily grow into a depression or over an elevation. The first requisite, then, is to have the surface of the granulations on the same level as the skin. If the wound is deep and slow to fill up, a stimulating dressing, such as tincture of myrrh, one part to sixteen of water, balsam of Peru, or balsam of copaiba, may be used. When the level is gained, an ointment, such as zinc oxid or boric acid ointment, should be applied for the double purpose of protecting the tender granulations and of keeping the edge of the skin soft and preventing scab formation, or silver foil or Cargile membrane may be laid on so that the delicate new epithelial cells have a better opportunity to multiply. When the granulations grow too rapidly and are raised above the level of the skin, they should be removed. If the elevation is but slight they should be cauterized with burnt alum or silver nitrate (I prefer a 50 per cent. silver nitrate solution applied with a cotton swab, to the solid stick, because it is less apt to wound the surface and make it bleed). Care must be taken not to allow the solution to spread farther than it is needed. If the granulations are very exuberant the most satisfactory method is to remove them with a pair of scissors held parallel to the surface and swab the bleeding base with silver nitrate solution. Fresh granulations are very quickly formed after cauterization, and at a lower level. A dressing of ointment should be applied as before. The dressings need not be frequently changed, since the pus on the gauze acts as an ointment in protecting the granulations and keeping the edges soft, and there is no danger in reinfecting a healthy granulating wound. Pus, however, if kept in contact with healthy skin for too long a time will macerate and excoriate it. The frequency of dressing may be determined by the condition of the surrounding skin rather than the amount of pus discharged. In the revision of the dressing the neighboring skin should be gently cleansed (warm water and some plain white soap do very well, care being taken not to cause bleeding), the granulations treated, and either a stimulating dressing or an ointment applied as indications require. The farther new epidermis progresses from the old, the less vitality it possesses, the slower it grows. New skin will not cover well more than one inch from the margin of the old. In wounds more than two inches from skin to skin, epidermatization can be brought about, and in smaller wounds hastened, by a plastic operation, or by skin-grafting either by the Thiersch or Reverdin method. These operations will be described elsewhere.

SHOCK.

Reaction from shock may be expected in from one to twenty-four hours after the injury. (See "Shock," p. 922.)

AIR EMBOLISM.

In wounds of large veins, such as those of the neck and sinuses, air may enter directly, passing to the heart, causing serious, even fatal depression of this organ. The reasons for this are, first, the heart is stimulated to automatic contractions very largely by the presence of fluid in its chambers, and, secondly, the heart is able only imperfectly to empty its chambers of air. Complications from this cause are much less frequent than is commonly supposed. (See chapter on Thrombosis and Embolism, p. 452.)

FEVER.

Slight aseptic wounds are not followed by febrile reaction. More severe wounds, especially where there is considerable hemorrhage into the tissues and injury to the tissues themselves, often cause a rise of temperature. This is due to the absorption of the blood ferments and devitalized tissues. The fever comes on a few hours after the receipt of the wound or after reaction from shock, if that be present. The temperature is not usually high, but may reach 102° to 103° F. The fever rapidly reaches its height and slowly but gradually declines. There is no chill and the constitutional symptoms are very mild. This form of fever is called aseptic or traumatic fever, and is frequently present in aseptic subcutaneous wounds, such as fractures, and requires no treatment.

If bacteria of putrefaction have gained entrance and set up decomposition in the blood-clot or necrotic tissues, the absorption of their product will cause a more violent and prolonged fever, often associated with chills. If such wound be opened and cleaned out the temperature will rapidly fall to normal. This fever is termed sapremia or septic intoxication.

Pyogenic organisms in a wound set up "suppuration fever." The bacteria may remain local in the wound, only their products being absorbed, or the bacteria themselves may be absorbed by the lymphatics and enter the blood, or they may enter the circulation by infecting a thrombus in a vein, which, becoming loosened, carries them into the circulation. In suppuration fever the temperature begins to rise usually on the second or third day and is accompanied by malaise and sometimes by a chill. The wound shows signs of inflammation, and if open pus will exude.

The local treatment of these infected wounds has already been described, and the pathology and constitutional treatment will be given in a special chapter.

In malarial districts occasionally chills and fever will come on shortly after a wound and cause some difficulty in diagnosis. I have seen a patient with a compound fracture of both bones of the leg develop chills and fever on the third day. The differential diagnosis is made by the lack of signs of inflammation in the wound, by the absence of leukocytosis, and by the regularity of the chills, but most conclusively by finding the specific organism in the blood, and the effects of quinin.

Occasionally after surgical operations a fever associated with a scarlatinal rash followed by desquamation occurs. This is possibly a rash due to pyemia or septicemia, but in certain instances is probably a true scarlet fever, from the entrance into the wound of the specific virus; at other times it is undoubtedly due to a peculiar idiosyncrasy to the dressings, such as iodoform or bichlorid of mercury, which have been used.

The passage of sounds or other instrumentation of the urethra is frequently followed by a chill and fever, which is called "urethral fever." The symptoms may be slight and last but a few hours, or there may be repeated chills and high fever. It has been suggested that this phenomenon is due to nervous influences, but in all probability it is due to infection through a slight wound in the mucous membrane.

Hysteria alone may give an actual rise in temperature aside from any deception on the part of the patient. Some of the highest temperatures on record have been due to this condition. As a rule, a diagnosis of hysterical fever can be made by the lack of other cause of fever, and finding other evidences of hysteria. Great care should be used, however, in ascribing fever to nervousness or hysteria, lest a more serious cause be not overlooked.

Some independent intercurrent diseases, as pneumonia, typhoid, tonsillitis, etc., may give rise to fever. All these conditions should be kept in mind and carefully considered in any fever following wounds and injuries.

SEQUELS OF WOUNDS.

The commoner sequels of wounds, sapremia, septic infection, pyemia, gangrene, tetanus, osteomyelitis, etc., will be described in their proper chapters, but there are certain other conditions which will be briefly mentioned.

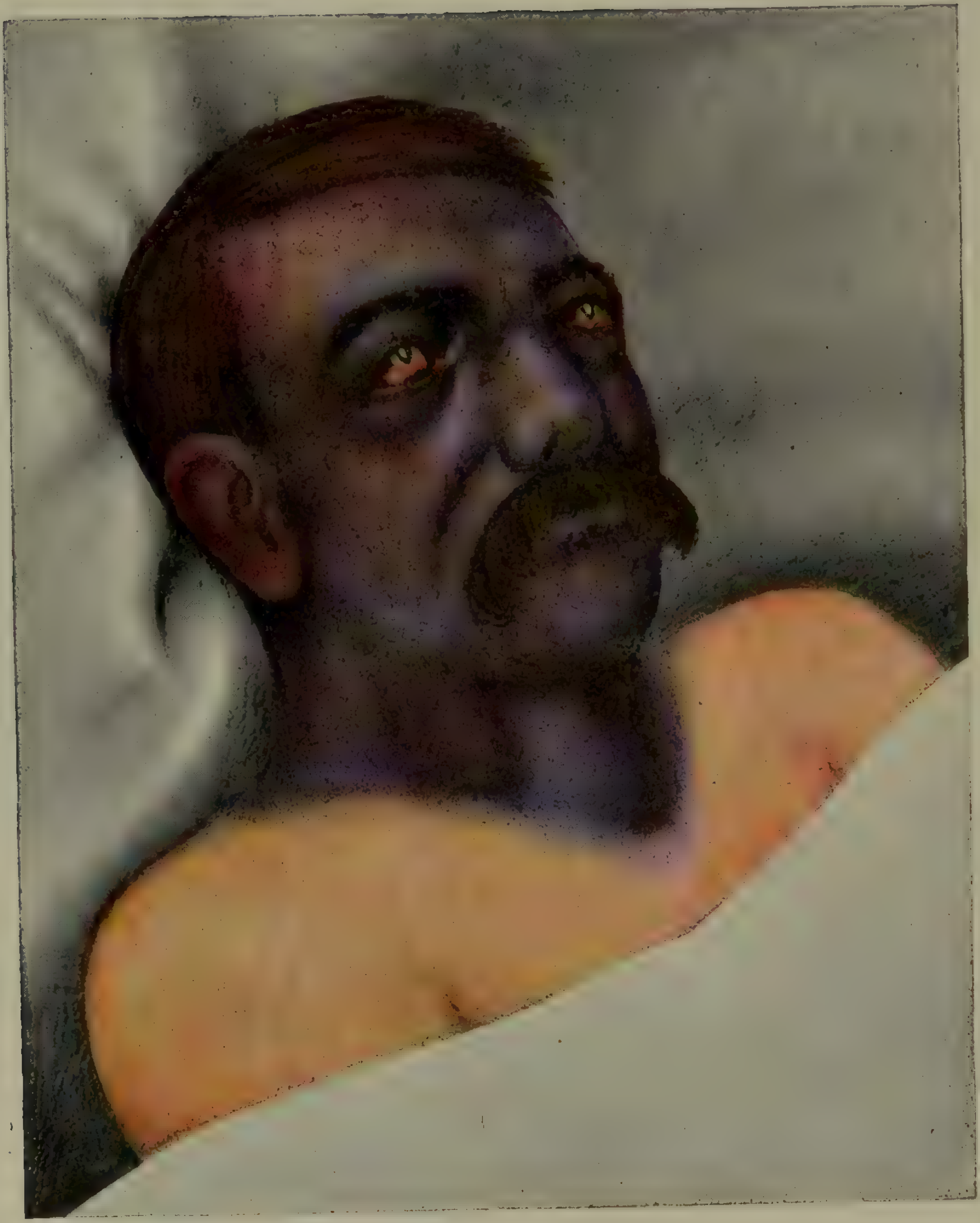
Aneurism.—Following an injury to an artery any of the various forms of aneurism may result. There are two forms, however, which are nearly always caused by trauma. These are the false and the arteriovenous aneurism. A false aneurism is one in which there is a leakage of blood from a wound in an arterial wall, the blood remaining fluid and exciting the tissues to the formation of a fibrous wall about it, producing a fibrous sac in communication with the lumen of the artery. None of the coats of the artery are present in the wall of the sac.

An arteriovenous aneurism is one in which there is an abnormal communication between an artery and a vein. These two forms of aneurism are prone to follow wounds, and especially punctured wounds.

Bickham [4] reports a typical case of arteriovenous aneurism. A man was shot in the thigh by a pistol ball. The bullet traversed the muscles, wounded both femoral artery and vein, and lodged in the bladder, from which it was voluntarily passed. Ten days later he was admitted to the hospital with an arteriovenous aneurism in the groin, two by two and one-half inches. The case was subsequently cured by ligation of the external iliac artery.

The treatment of traumatic aneurism is the same as that of non-traumatic and will be described in another chapter.

PLATE XVIII.



TRAUMATIC ASPHYXIA.

Discoloration following forcible compression of the thorax (Beach and Cobb, in "Annals of Surgery," April, 1904).

Myositis Ossificans Traumatica.—A condition of chronic inflammation of the muscles after prolonged irritation, such as "cavalryman's bone" in the adductors, is not very rare, but cases of ossification are reported after a single blow, as a kick from a horse. The osseous tissue may be found as early as two weeks after the infliction of the injury. At the seat of a severe contusion a tender swelling persists with more or less interference with the function of the muscle. The swelling, as a rule, increases progressively in size. Microscopically an area of chronic inflammation will be found in which are embedded spicules of bone. The bone arises in the muscles itself and not from the periosteum. The treatment of this condition is excision of the affected area.

Traumatic Asphyxia.—This is a rare condition of the face and neck which sometimes follows severe injury of the thorax and abdomen. After a compression of the trunk which has lasted sufficiently long to prevent respiration for an appreciable length of time, there appears on the face and neck a bluish appearance which resembles deep cyanosis, and associated with it subconjunctival hemorrhage. The discolored area includes the scalp, face, and lips, and extends a varying distance down the neck and chest. In a case reported by Birge, of Cleveland, it extended to the nipples. In one reported by Beach, of Boston, it extended to the root of the neck in front, but in the back formed a diamond-shaped outline following the edge of the trapezius muscle and about one inch internal to it. (Plate XVIII.)

On close examination of the affected area it is seen to be composed of numerous dark blue or reddish-blue areas from one-half to one millimeter in diameter, irregularly placed, leaving narrow zones of normal skin between them. On pressure the bluish color diminishes but does not disappear, and slowly returns on relief of pressure. Under the conjunctiva there is a true hemorrhage, bulging that membrane forward.

Of the reported cases, all were young, from fifteen to thirty-five years of age.

As recovery progresses the color fades without going through changes seen in an absorbing subcutaneous hemorrhage. Under the conjunctiva there is a true hemorrhage and these changes of color take place. Many cases have been seen post-mortem in persons who have been crushed to death in crowds, but the pathology has not been satisfactorily established. In Beach's case pieces of skin were excised from the back of the neck and examined microscopically. All sections showed apparently normal skin. From the clinical course and the microscopic findings it seems probable that the condition is due to dilatation of the capillaries, with stasis of deoxygenated blood, without extravasation except under the conjunctiva. Hueter, from his experiments on rabbits, comes to the same conclusion. Perthes concludes that the limitations of the discoloration to the face, neck, and upper chest is due to the lack of competent valves in the veins of these regions. The cases of recovery have all been in young adult life, probably because in the aged, with more rigid vessels, the severe compression causes death.

Keloid.—In certain individuals, and especially in certain races,—

the negro, for example,—scars in the skin tend to hypertrophy enormously, forming at times large tumors of dense scar tissue along the line of old wounds. This condition is most apt to follow lacerated wounds where accurate apposition of the skin has not been made and there is normally considerable scar tissue formed, and is least in incised wounds with a minimum of scar. The cause of this peculiar overgrowth is not known. The treatment is difficult. If the tumor is removed, a second keloid may form in the scar of the incision. The operation scar can, however, be made small and the edges closely approximated so that the tendency to this formation will be less. The non-operative treatment consists in the administration of thiosinamin, preferably by subcutaneous injection. In certain cases this drug seems to have a remarkable effect in causing the absorption of scar tissue. Some cases have been cured by the x-ray.

Vicious Contractions. — Large superficial scars, especially those from burns, frequently cause great deformity by their contraction. This is especially true when the scar exists at the flexure of joints. Large scars on the anterior aspect of the neck may depress the skin and bind it to the chest; scars at the bend of the elbow or wrist may cause permanent flexion of these joints. Such contractions do not follow even extensive wounds unless there has been a destruction of tissue involving at least a portion of the true skin. Prophylaxis is of great importance. In wounds in which there is a large loss of integument the amount of scar tissue should be reduced as much as possible by applying Thiersch grafts; where the wound is over a joint the member should be kept on splints in an extended position. If vicious contraction has taken place the condition may be improved by some plastic operation, such as excision of the scar and filling the defect by a sliding operation or applying Thiersch grafts. Details of the operation will be given in the chapter on plastic surgery.

Tumors.—The relation between trauma and tumors is a much discussed question. Almost any individual who suffers from a tumor can recall an injury to the part affected, at some time in his life. Nevertheless the number of tumors which follow injury so closely that some connection is probable is quite large. Ziegler[7] gives a table of 1850 cases of carcinoma and sarcoma, of which 268, or 14.5 per cent., apparently followed a single trauma. In another table of 1628 cancers of the breast, 214, or 13.1 per cent., followed a single trauma. The length of time after the trauma that the tumor has appeared has varied from eight weeks to seventeen years. Considering the number of injuries which occur to every individual and the comparatively small number of persons affected by malignant tumors, the percentage of injuries which directly lead to the formation of malignant growths must be very small. Whatever may be the relation of trauma to the development of carcinoma, the speedy growth of sarcoma of bones not infrequently following blows or contusions of the scalp, long bones, or the ilia, leaves no doubt as to their direct connection with and dependence upon traumatism.

Nervous Affection and Mental Disturbances. — Aside from such nervous diseases as neuritis and paralysis from direct injury to nerve-trunks or the spinal cord there are various conditions of hysteria and neurasthenia following injuries. These diseases may occur after a railroad accident, even without, or at most after a very slight injury to the patient. These traumatic neuroses will be described in their proper section. It may be said, however, that they are more frequently cured by the settlement of the suit for damages, which usually accompanies and aggravates them, than by any form of medical treatment that may be instituted.

Jacksonian epilepsy is a condition which follows injuries to the head, chiefly contusions of the brain and depressed fractures. Mental disturbances may follow injuries of the head, especially fractures of the base or vault. Among 18,608 cases of insanity, 480 were found to be due to cranial injury.[8] Stolper approached the subject from the other side, and found that 981 cases of cranial injury were followed by mental disturbances in 12 instances. This subject will be fully treated in another chapter.

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II. CONTUSIONS.

A contusion is a traumatic solution of continuity of tissue without causing a complete anatomic separation. The wounding force compresses, displaces, and irregularly disrupts the histologic units. A contused wound may be regarded as an irregular *histologic* solution of continuity, while a lacerated or incised wound is an *anatomic* solution.

Contusions, lacerations, and incisions are in many instances variously combined, the designation being given from the predominating character. Wounds may be described, according to this predominance, as lacerated and contused, or contused and lacerated, incised, lacerated and contused, etc. When the violence is applied at the point of contusion, as a blow from a fist, it is designated *direct* violence; when the contusion is produced at a distance, as falling upon the hand, causing contusion of the shoulder, there is *indirect* violence.

Causes.—Contusions are caused by a more diffuse application and by a milder degree of violence than that causing lacerations. Falls, fist blows, kicks, the passage of wheels of vehicles over the parts, are common examples of the cause.

Phenomena.—Locally there is usually swelling, pain, and subcutaneous hemorrhage. The swelling is caused by hemorrhage, the pouring out of lymph, and the interference with the circulation. The swelling appears directly after the injury, of which the welts from a lash and blows upon the head are examples.

Pain.—Immediately upon the receipt of a severe contusion the injured part may be stunned into numbness, but this is soon followed by a dull, throbbing pain, which later may develop into acute pain of great severity. The severity of the pain depends in a great measure upon the susceptibility to it of the injured person, and this in turn may be largely influenced by his nationality, temperament, and state of health. It is also naturally very largely dependent upon the location of the injury, and the tissues involved; as illustrations may be instanced the sickening pain from a blow upon the testicle, the tingling pain in nerve injuries, and the intensity of pain in parts like the finger-tip, richly supplied with nerves, as contrasted with similar contusions of the back, in which the nerve-supply is scanty.

Hemorrhage.—In most contusions there is subcutaneous hemorrhage, ranging from a few drops of blood from the rupture of the minutest vessels to extensive diffuse hemorrhage. The discoloration attending contusions is due to hemorrhage. This discoloration is termed suggillation or ecchymosis. Ecchymoses can be differentiated from congested areas by the fact that, the blood being outside of the vessels, the color does not disappear on pressure.

If the blood collects in one place in the tissues, pushing aside the tissue elements and forming a single large cavity filled with blood, the tumor is called a hematoma. In such a hematoma the blood may or may not clot. Effusion of blood from contusions into certain of the natural serous cavities of the body, such as the tunica vaginalis testis, is termed a hematocele.

If the hemorrhage be so superficial as to permit the absorption of oxygen, the color is red; but if it be deep, it is black; if mixed with other fluids, the depth of color is proportionately lessened. In certain tissues if the hemorrhage be progressive the anatomic parts may be widely separated, as, for example, in scrotal or spermatic cord hemorrhage, and it may then be designated a dissecting hemorrhage. Hemorrhage may be so extensive as to cause constitutional symptoms. In the region of the orbit, the scrotum, the retroperitoneal tissues, etc., hemorrhage is apt to be progressive because there is little resistance offered to the flow. Very small vessels may discharge a surprisingly large amount of blood. Hemorrhages under fascia, as that underneath the fascia of the lower back, sacrum, loins, and thigh, sometimes terminate peculiarly, in that even after the actual hemorrhage has ceased the bulk of fluid is increased by the discharge of serum into it. The pressure and the reaction of the tissues to free blood may form a distinct wall consisting of exudate with round-celled infiltration, which later becomes organized into a distinct membrane. In such cases it tends to become a permanent tumor.

Terminations of Contusions.—Slight contusions terminate promptly by resolution; the more severe may terminate in gangrene, inflammation and abscess, fibroid thickening, hypertrophy of the tissues involved, in the case of bone or cartilage, chronic inflammations, osteomyelitis, and even malignant growths, particularly sarcomata.

Prognosis.—The prognosis of contusions is a matter of everyday importance, and it is sometimes extremely difficult to make accurately. The determining factors are principally the nature and violence of the contusing force, the tissues and organs involved, and the general condition of the patient. Even the injury of the tissues that may be easily inspected, such as the skin, may be much more severe than is apparent. In tissues of low vitality, such as the synovial membrane, cartilage, and ligaments of a joint, repair is proportionately delayed, whereas in highly vascular tissue it is more rapid. Contusions of tissues that cannot be given physiologic rest, such as the thoracic wall, respiratory muscles, etc., respond less promptly to treatment.

The general condition of the patient is an important determining factor in a prognosis, the most favorable being vigorous adult life without organic disease. Among the unfavorable general states are the extremes of life, the very anemic and the plethoric, the tuberculous, the syphilitic, the scorbutic, the diabetic, and like states, while in the rheumatic and the gouty the slightest injury may be most persistent. The starved, the over-fed, the over-worked, the fatigued, the alcoholic, and extremes of heat and cold are to be considered as unfavorable cases. Patients having suppurative processes, such as empyema, etc., show a decidedly greater tendency toward termination in abscess.

Treatment.—Slight bruises favorably located require no treatment. The arrest of hemorrhage, thereby diminishing the swelling, pain, and discoloration, is important. If the hemorrhage be from small vessels, elevation, rest, and the application of ice are sufficient. Frequently the application of pressure is indicated. A familiar example is the control of the bump on a child's head by pressing upon it the handle of a cold spoon or a piece of ice, making a combination of pressure and cold.

Hemorrhage in deeper parts, such as that occurring under the fascia of the thigh or of the back, is sometimes best controlled by adhesive strapping. If the vessels are large and hemorrhage is rapid, it is sometimes necessary to make a free incision and apply a ligature. Evaporating lotions or elastic pressure by bandaging over absorbent cotton may assist. If the hemorrhage be in a joint, causing immediate painful swelling from distention, prompt aspiration will give relief. This should only be resorted to under the strictest aseptic precautions, as the conditions are most favorable for microbic growth. The prevention of, or minimizing the formation of a black eye following a blow is best accomplished by means of pressure and ice. If the soft parts are so severely contused as to jeopardize the nutrition, both bandaging and ice should be withheld, and in some instances even warm applications are advised. After the acute symptoms have passed judicious massage may be most helpful in securing early resolution. Restoration of the vasomotor tone when impaired or lost may be greatly facilitated by douching with cold and hot water alternately, followed by massage.

While, during the acute stages, physiologic rest is important, the restoration of functional use in severe cases must be tentative, guided by the response of the tissue in the form of increased pain or swelling. These phenomena should be avoided if possible. If hematomata be not absorbed they should be aspirated and pressure applied before structural changes take place, such as the formation of a membrane. If the latter occurs and a sufficient time has elapsed for the formation of definite new tissue, aspiration may be followed by obliteration of the sac. In some instances it is necessary to make a long incision and dissect out the entire sac wall to effect a permanent cure. Sometimes hematomata become so thoroughly and firmly organized, and gradually increase in size with all the characteristics of a solid or semi-solid permanent tumor, that it is extremely difficult to differentiate them from new growths. Such hematomata have even been removed under the impression that they were new growths. In such dissections a rather unusual amount of hemorrhage may be encountered. If pain and tenderness persist for a long time, particularly if there be a predisposition to tuberculosis, especial care is required. If after a comparatively slight contusion temporary recovery follows, then later some pain and tenderness with local heat appear, one is quite justified in assuming that the contusion served as the cause of a *locus minoris resistentiæ*. A slight injury may determine the subsequent development of a tuberculous focus.

In young children and in old age, in the anemic, in the plethoric, in the dissipated, the diabetic, the scorbutic, and in subjects of general lowered resistance the treatment of contusions should be continued until thorough and complete resolution is assured before relaxing the closest observation.

CONTUSION OF PARTICULAR REGIONS AND TISSUES.

Skin.—The resistance of skin to traumatism is often extraordinary. The wheel of a railway carriage may pass over a leg, completely crushing the muscle, blood-vessels, nerves, bones, in fact, may virtually separate the limb with the exception of the skin, which may not show more than local discoloration and abrasion. A blow upon the head may cause a comminuted fracture of the skull and yet the scalp remain intact. It is very difficult indeed to form an estimate of the subcutaneous damage from inspection of the skin, yet this same skin which does not suffer a solution of continuity may have lost all its vitality by the wounding force and gangrene follow. Such skin, if used as a portion of a flap in amputations, usually becomes gangrenous.

Muscle.—Muscles are rather easily torn and often pulpified within their sheaths.

Bone.—The most important consideration in contusions of bone is the possibility that by the lowering of the resistance the part may become the focus of pyogenic or tuberculous infections. Not infrequently even in an apparently healthy individual there are pyogenic organisms and even tubercle bacilli in the circulating blood. While the body is in a state of normal health these organisms are unable to localize and multiply, but when they encounter an area of lowered resistance they are apt to lodge and set up inflammatory processes. This is especially true in contusions of bone. After such contusions osteomyelitis, periostitis, etc., with all their serious consequences may occur. It has been noted that after severe contusions infections by pyogenic organisms more frequently occur, while tuberculosis is more apt to follow injuries so slight as frequently to be overlooked.

Nerves.—Contusion of nerve-trunks is often a matter of greatest importance on account of the neuritis which may follow. A blow upon the arm over the circumflex or upon the elbow involving the ulnar may be followed by an intractable neuritis lasting for years. Blows upon the shoulder may involve the articular branches supplying the joint, causing thereby changes in the nutrition of the articulating surfaces and capsule, accompanied by great pain and atrophy of the muscles and of the joint itself, producing a marked disability over a long period of time. The duration may correspond to the length of time required for the regeneration of the nerve. In gunshot wounds of nerve-trunks a neuritis may endure a lifetime, and the late consequences, which have been so admirably studied by Mitchell, Moorehouse, and Keen, may modify, and even destroy, the usefulness of the patient. I have seen a contusion of the sciatic nerve from a revolver wound, in a strong healthy adult subject, causing a neuritis which continued many years.

Blood-vessels.—In contusion of blood-vessels their walls may be so weakened at the point of impact as to be followed by an aneurism.

Head.—The immediate effect of contusions of the head may be direct and local, indirect and regional, and remote. Among the interesting local effects are contusions that crush the scalp at the point of contact, following which there is immediate swelling at the periphery of the injured area, thus giving the impression that there is a depressed fracture of the skull. If a severe contusion is located in the temporal region, and in addition to the crushing of the skin the temporal muscles suffer as well, perhaps even the temporal fascia, an immediate examination may entirely deceive the inexperienced into believing that he can palpate the margins of a depressed fracture. Such contusions of the skull may sometimes be attended by local and even intracranial suppuration. In the latter event the infection probably passes along the vessels through the skull.

Among the indirect effects of contusions of the head are contusions by contrecoup of the brain, injuring this tissue, rupturing small vessels or even large ones, causing a sufficient amount of pressure to produce serious symptoms and even death.

Among the later sequels of such injuries may be mentioned traumatic neurasthenia, headache, and Jacksonian epilepsy. In every contusion of the head it is well to regard the possibilities as grave until they are proved otherwise. One must exclude fractures, minute injuries of the brain, small, and even large, hemorrhages. Should local suppuration follow a contusion, the remote and grave consequences of an infection must always be borne in mind. In luetic subjects and in those reduced by wasting disease, or those who at the time are suffering from suppurative processes elsewhere, it is well to bear in mind the added probability of infection. This occasionally appears as a localized osteomyelitis, caries, or necrosis. Aside from the histologic and anatomic injury, the immediate effect of contusions of the head upon the function of the cerebrum, cerebellum, and medulla is often a matter of important and grave immediate physiologic consequence. A contusion may cause immediate though temporary loss of consciousness. The subject may be stunned. Then, again, if the injury is over the cerebellum, momentary ataxia, dizziness from modification or temporary loss of function of this organ, may follow. The motor area may likewise be temporarily modified or inhibited, causing complete loss of voluntary movement and power. Such a contusing injury, too, acting upon the medulla, may cause a temporary inhibition of respiration, of the heart's action, or of the vasomotor centers. That is to say, the vital centers of the medulla may be so temporarily modified or inhibited as to threaten, and in rare instances may cause, instant death. Likewise, the special senses may be modified, as momentary blindness, "seeing stars," following stunning blows. A similar modification in the special sense of hearing following a contusing blow, spending its effects upon the auditory centers, may occur. The majority of such effects are fleeting, or at least of but short duration. Sand-bagging has often caused death though meant only to stun. Blows delivered upon the occiput or upon the upper portion of the neck are more apt to cause the dangerous or even fatal inhibition of the vital centers governing the circulation and respiration.

The Eye.—One of the most obvious and common contusions is that of the orbit or its immediate vicinity, causing the well-known "black eye." This discoloration, as previously stated, is due to interstitial hemorrhage. The hemorrhage into the conjunctiva remains red because an exchange of oxygen takes place; in the orbit, black, because the hemorrhage is too deep for such exchange. If there is a local accumulation of blood, a part at least may be drawn off with a fine needle. The application of cold, in the form of cold cloths or ice-bags, with some pressure, is most useful in arresting hemorrhage. The reabsorption of blood is perhaps best facilitated by skilful massage after the acute hemorrhage has ceased. The use of leeches is unsurgical and should not be resorted to.

Face and Neck.—Contusions of the face other than that of the eye present no special features, but it is always well to remember the indirect effect of the contusing blow, especially of the lower jaw, upon the brain and medulla. The transmission of such violence to the base of the skull may be sufficient to cause fracture, hemorrhage, contusion, or laceration of vital importance, causing either temporary inhibition or death.

In contusions of the neck, those of the larynx are of the greatest importance. In this instance, too, immediate inhibition of the respiration and of the circulation may be produced, though in a wholly different manner. This is due either to the direct influence upon the trunk of the vagus, or more commonly to the influence of the superior laryngeal nerve, causing an inhibition reflexly. Direct contusion of other structures in the neck, such as the blood-vessels, phrenics, hypoglossals, fascia, tendons, and muscles, is of less importance. It is well to remember certain exceptional injuries, such as the hematomata of the sternomastoid in the new-born, the injury or even tear of the brachial plexus, with their long train of neuritis, paralysis, and atrophy, which may follow.

Chest.—In contusions of the chest the effect may be local and direct or regional and indirect. They may involve the histologic and anatomic parts with the disturbance of physiologic function. Direct blows upon the chest are numerous, causing the usual local symptoms. The indirect effect of a contusing blow may be a fracture of a rib or laceration of a blood-vessel, laceration of the pleura or of the lung, causing hemorrhage of more or less importance. Light contusions of the chest may become infected and suppurate, or may result in a tuberculous focus, but they rarely involve the intrathoracic region. The indirect effect upon the organs contained in the thorax is of more importance than the direct local effect. The most important immediate effect of such contusions is due to a modification of the physiologic action of the heart or of the lung upon respiration; a common example is the inhibition of the diaphragm from a blow in the pit of the stomach or upon the short ribs. However, the effect upon the heart itself is a matter of the greatest importance. (This is more fully considered under Surgical Physiology of the Thorax, p. 103.) When the heart itself is subjected to traumatism either direct or indirect, it may cause arrhythmia or immediate arrest. The effectiveness of the so-called solar plexus blow upon the short ribs is due entirely to the mechanical interference with the heart as a muscle, and upon the diaphragm, the solar plexus having no part in its causation.

In experimental research and in autopsies there is found in a surprising number of instances physical damage to the heart itself. In a larger proportion of instances than one might suppose, also, the lung tissue has been torn, frequently an interstitial tear which cannot be noticed except on close observation. It will be noted that in the majority of instances in which violence upon the lower ribs causes collapse or death the violence has been wholly unexpected, such, for example, as the deaths recorded by striking the floating ribs against the corner of a table while walking in a dark room, or in the case of drunken men with complete relaxation in falling, etc. That is to say, under circumstances in which no muscular resistance is offered, permitting the driving in of the ribs, traumatism of the heart and lungs is more likely to occur.

Abdomen.—Contusions of the abdomen have been extensively studied and the literature contains many exceptions to early recovery. A contusion caused by considerable force in this region must be considered important until proved innocent. The effect upon the abdominal wall, because it is so readily yielding, is not so marked as that of the soft parts covering the skull, or of the thorax. However, not infrequently contusions of the abdominal wall are attended by rupture of the muscles, hemorrhages, and in some instances the formation of an abscess.

The indirect violence to the contained organs is a matter of supreme importance. A contusion in the region of the stomach in cases in which a gastric or duodenal ulcer is on the point of perforating, may complete it. In one instance I observed a tear of the duodenum by the driving in of the eleventh rib, in a severe contusion of this region.

Spleen.—It must be borne in mind that the spleen is a friable organ, and when subjected to violence is readily lacerated. Its position, lying as it does mainly underneath the arch of the more mobile ribs, offers a measure of protection against external violence, provided such violence is not sufficient to catch it between the depressed ribs and the vertebral column. In contusions of other portions of the abdomen the force of the violence is spent in all directions; the spleen receives only a part, and, lying next the movable diaphragm, is still further protected against even this force by the upward yielding of this organ. The chief significance in injury of the spleen is the accompanying shock and hemorrhage. There is but slight tendency toward spontaneous arrest of hemorrhage. Any solution of continuity, then, of so vascular an organ with so little contractility or elasticity, with slight tendency to spontaneous arrest of hemorrhage, must be viewed as important.

Kicks, blows, etc., in the region of the spleen have in a considerable number of cases caused fracture of this organ, followed by dangerous, even fatal hemorrhage. A striking example of this came under my notice at Camp Alger, in which a private was kicked by a mule, causing, so far as could be observed, but a simple contusion of the abdominal wall. He soon showed evidence of severe internal injury and hemorrhage. An immediate laparotomy was done, the spleen was found shattered, and the abdomen filled with blood.

Liver.—Contusion of the liver is quite analogous to that of the spleen. It lies between the elastic costal arches and the solid vertebral column, protecting it against lighter blows, but exposing it to direct compression if the blow is heavier. Its tissue is friable, extremely vascular, and contains but a small amount of connective or elastic tissue, thus leaving it with but few of the factors for the spontaneous arrest of hemorrhage. Heavy blows in this region should always arouse a suspicion of a hepatic lesion. A blow that ruptures the liver is apt to be attended by less shock and collapse than one that ruptures the spleen. This difference may, I think, be accounted for from the fact that, the spleen being a smaller organ, the ribs may be driven farther down, injuring the heart, the diaphragm, and the large splanchnic nerves, while on the right side the liver itself receives more of the brunt of the force.

Kidneys.—The kidneys occupy a somewhat analogous position, lying also in close apposition to the spinal column and partially protected by the movable ribs. Their parenchyma being friable, they are often lacerated in a manner similar to that of the liver and spleen. Lying as they do behind the peritoneum, hemorrhage is usually less grave than in hemorrhage of the abdominal organs, but the extravasation of urine with its destructive effect locally and its toxic effect constitutionally, together with the hematuria, makes such injuries frequently dangerous and sometimes fatal.

Pancreas.—The pancreas has but little natural resistance and is occasionally ruptured by the application of a heavy force. The force required for rupturing this organ must always be very considerable, because it probably does not occur unless the violence is transmitted quite directly through the anterior wall, pressing it against the spinal column. Lacerations of the pancreas are usually attended by very considerable shock as the most important immediate result. The discharge of the destructive pancreatic juice into either the greater or the lesser peritoneal cavities may cause a serious complication. If the patient recovers from the immediate effects, a retroperitoneal hematoma or a pancreatic cyst is likely to follow. Most instances of rupture are due to such contusing forces as the passing of a wagon-wheel over the middle of the body, or being crushed between railway cars, etc.

Intestines.—Contusions of the abdomen may cause injury of any portion of the intestinal tract. My associate, Dr. Lower, observed a case of a ship carpenter, who was struck a glancing blow upon his rather pendulous abdomen by a falling plank, and, feeling rather upset, went to his home. He was there seen and grave internal lesion was diagnosed. He refused immediate operation. At the autopsy it was found that there was a perforation of the ileum. There was no evidence of previous ulceration at the point of injury or at any other point in the alimentary tract. The patient was at the time of the accident apparently in normal health.

In another instance under my observation an iron-ore bucket fell, striking a heavy glancing blow upon the abdomen of an ore handler, knocking him over. He was in considerable shock, and at the operation, done several hours later, it was found that the mesentery of eighteen inches of the transverse colon had been entirely separated from its attachment, completely destroying its blood-supply. The mesenteric vessels were also freely bleeding.

In a personal experience in 2600 abdominal sections but three operations were performed for rupture of otherwise healthy intestines from contusions of the abdomen.

The urinary bladder is less frequently injured by ordinary contusions of the abdomen than any other of the viscera, largely because of its being shielded by the firm pelvic arch. Its injuries are chiefly due to fractures of its imperfect bony cage.

Unless specially distended and diseased, the gall-bladder is not apt to be torn.

Every contusion of the abdomen of considerable force, then, must be viewed as grave until proved innocent. If hemorrhage and perforation cannot be excluded, and if the surroundings are favorable, it would be much safer to make an immediate exploration.

Back.—Contusions of the back, while usually far less grave than those of the abdomen, thorax, and head, still have their own significance, the most important being the indirect violence to the spinal cord, causing temporary shock and hemorrhage. Every indirect violence of the cord, like that of the brain and the heart, may cause temporary suspension or modification of its function. Paresthesia, momentary paralysis, loss of control of the sphincters, may be mentioned. If important symptoms develop later, hematomyelia, must be considered. The analogy here for surgical treatment does not hold, as in the case of the head and abdomen, as immediate operative measures must be very carefully considered and are rarely indicated. In this instance it is assumed that there has been no fracture and no compression.

It is these cases of contusion of the back that lead to so many difficult medicolegal cases. After very slight injuries which could hardly seem sufficient to cause any gross pathologic lesion many cases of spinal symptoms occur. This condition is often spoken of as "railroad spine," "traumatic neurasthenia," etc., and will be fully discussed in a separate chapter.

Hemorrhage underneath the dense fascia sometimes becomes a matter of great importance, not because it is a risk as such, but because it tends to dissect its way along the line of least resistance, forming in some instances a very large hematocele, which if left to itself not only may not become absorbed but may increase in size and continue the pathologic dissection almost indefinitely. The reaction of the surrounding tissues results in the formation of a membrane-like cyst wall, which presumably secretes serum. If the accumulation of blood be allowed to remain until such membrane formation, it may become extremely resistant to treatment —as aspiration, injection of iodin or carbolic acid, strapping under pressure with complete rest, and even permanent drainage.

In four instances I have been obliged to dissect out the entire sac. In the first instance I dissected out only the external half of the sac, believing that adhesion of the new tissue, if pressed firmly against the membrane opposite, would take place. On the contrary, the sac refilled and I was obliged to operate again, this time completely removing the sac, after which healing was prompt.

Perineum.—Contusions of the perineum, like contusions of most other regions, derive their greatest importance from a possible injury of the deeper structures, such as the urethra and the prostate. In the case of the latter, retention of urine from swelling or abscess may follow. The urethra is sometimes completely torn across. In three such cases Lower successfully sutured the divided ends. It is a matter of the utmost importance to act promptly in any case of contusion of the perineum, should it be complicated by rupture of the urethra, since the absorption of urine, the local irritation, and the almost certain infection constitute great dangers. The exact diagnosis, if in doubt, may readily be made by the use of the urethroscope. Free incision is, in such cases, indicated. Occasionally a subcutaneous hemorrhage which tends to be progressive may demand surgical attention.

Testicle.—In case of hydrocele, contusion of the testicle not infrequently causes a very large hematoma, and hematocele, sometimes amounting to a dissecting hemorrhage, causing the scrotum to assume a giant size with intensely black discoloration, the hemorrhage extending well up into the groin, even to the loin and lower abdomen. It may become necessary to make a free incision, turn out the clot, and secure the bleeding points. Even in the absence of a hydrocele severe hemorrhage may occur from contusion. The especial susceptibility to shock after contusions of this organ is well known.

Vulva.—Contusions of the vulva may be followed by extensive swelling, especially in cases in which vessels have been torn. The hemorrhage may become dissecting.

Extremities.—Contusions of the joints are matters of great importance, especially if the subject be tuberculous or rheumatic. In the former instance an acute process may be established; in the latter the process of repair is so slow that a slight injury of a rheumatic joint may cause months of pain and disability. The immediate swelling following contusions of the joints is for the most part due to hemorrhage; the lesser factor is edema.

I have in twenty instances made records of immediate aspiration of various joints presenting marked swelling immediately after contusion; in all these cases fluid blood was found and the swelling and intense pain were markedly modified. This, followed by firm elastic pressure upon a generous layer of cotton, with ice packs and absolute rest, has generally been sufficient to insure a speedy recovery.

Contusions of the bones and joints in children, particularly those inclined to tuberculosis, very frequently form the *locus minoris resistentiæ* for the implantation of tubercle bacilli.

Contusions of the knee-joint may cause a displacement of the cartilages, and detachment of fringes of the joint, leaving a joint long or even permanently disabled. A heavy contusion of the arch of the foot may by indirect violence cause so much damage to the supporting ligaments as to cause an acute traumatic flat-foot.

Contusions in general form an important class of injuries, especially from the standpoint of the indirect violence to the deeper tissues and organs. The immediate effect in the way of shock is more fully considered under that topic.

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III. SHOCK AND COLLAPSE.

Predisposing Causes.—Age.—When the tissues and organs are approaching the end of their life cycle, their vital forces almost spent, and senile changes established, there is a marked diminution in the physiologic response to trauma and an equal or greater diminution in the reserve vital force, and, hence, there is a diminution of the range of compensation of the nerve-vascular mechanism. The senile heart has an uncertain and limited range of action. The arteries are hard and the blood-pressure is high.

When aged patients are subjected to operation or injury, the immediate circulatory and other changes may be surprisingly slight, but under these conditions the power of compensation or rebound is quite likely to be equally slight.

There is probably no other class of patients so misjudged. In a number of such cases during operations I have had careful blood-pressure records made and have noted the discrepancies between these relatively accurate records and the clinical estimation of the anesthetist.

It is difficult to dissociate the hard senile radial pulse—which, with all the other soft parts atrophied about it, resembles a hard subcutaneous cord—from that of the adolescent and young adult, which is pliable and embedded in a rounded arm of soft tissue. Then again the senile blood-pressure is from 20 mm. to 30 mm. higher than that of young adult life. There is also a greater range of individual variation in the senile than in the young adult blood-pressure. In a given senile case the blood-pressure may have fallen to an unsafe level, yet may have only reached the normal pressure of the young adult. The circulatory status of senile cases should be studied individually and the pulse characteristics and blood-pressure changes should be interpreted relatively—only in terms of senility and with reference to the previously determined standard of the individual in question.

The aged only *apparently* endure operations well. The risk is determined not by the age of the patient but the age of the circulatory apparatus.

The operative risk in childhood is also greater than in young adult life. In the new-born, before the physiologic connections between the great divisions of the central nervous system have been established, it is quite probable that at least certain operations are very much more nearly shock-free than they will ever again be. They are not only shock-free but free from the appreciation of pain. In the new-born extensive operations for cleft palate are endured without anesthesia, pain, or shock, the only immediate risk being hemorrhage. Within a week or more these physiologic connections become established, after which the infant becomes even more susceptible to shock than the adult.

Among the reasons for this increased susceptibility may be mentioned: The tissues and organs being in the unfolding stage have not reached their maximum physiologic activity and are less competent than adult tissue; the nerve-vascular mechanism is extremely mobile, yielding maximum response to minimum stimuli. Adult life represents to a certain degree a survival of the fittest; the vitally unsuccessful are eliminated. In infancy the adult number of nerve-elements are packed in a very small area, while the surgeon's hands, many of his instruments, etc., are of adult size. Could the infant be operated on in its own ratio,—that is to say, by a Lilliputian surgeon with infantile instruments, etc.,—the exciting cause would be greatly diminished and shock correspondingly less. The physics of the child also plays a part. The external surface, hence surface exposure, bears a direct geometric ratio of disadvantage to the child. The circulation in the child is decidedly more taxed than in the adult; metabolism is remarkably active to meet the extraordinary demands of new growth and exalted functionation. Any interference, then, with nutrition works a double havoc in the child. For these reasons the child may not maintain a reserve force at all proportional to that of the adult. If this be true, its range of compensation is more limited. In early life we may say that in the new-born there is a short period of immunity, disappearing with the establishment of the through paths of the nervous system, after which the greatest susceptibility appears, which, in turn, gradually diminishes, reaching in young adult life the period of greatest resistance to shock, then diminishing gradually toward the completion of the life cycle, reaching the minimum at its close.

Sex.—Before puberty there is little or no difference in the susceptibility of the sexes. After this the nerve-vascular system of the female becomes less stable, especially at the menstrual period. Meanwhile the male from his freer environment grows more hardy.

From puberty to the child-bearing period the female is probably slightly more susceptible to shock. The child-bearing period brings an increased capacity for bearing pain and for contemplating crises with fortitude. The multipara, except during pregnancy, is usually a better surgical risk than either the primipara or the male of the same age.

During the development and evolution of the menopause the female again becomes distinctly more susceptible. This period once safely over, the female has entered upon a long unbroken period of quiescence and her resistance is increased. The male in the meantime has been subjected, if not to more work and worry, at least to much greater irregularity of habits, to the chronic poisoning of nicotine and alcohol, and to other excesses. Then, too, the man, during the period of quiescence of the woman, is carrying the greatest burdens of his career, and from this period to the end he is not so good a surgical risk as woman. In the latter there are fewer scleroses, chronic inflammations, luetic lesions, degenerations, sequels of overwork, dissipation, irregular habits, and no prostatic hypertrophy, etc., all of which render him a distinctly worse risk.

Finally, the woman is more trustful, more tractable as a patient, more hopeful, and, therefore, suffers less from the psychic factor of shock and is more amenable to treatment.

Nationality.—The more highly organized races are said to be more susceptible—the highly organized American is probably as susceptible as any. The tranquil oriental shows apparently less susceptibility than the occidental; the North American Indian and the negro, less than his conqueror. Among the races of the so-called western civilization, the Hebrew and the Irish show perhaps less resistance than the Scotch, German, or English.

Climate.—Patients subjected to operation or injury while in regions to which they are unacclimated show decidedly less resistance than when on their native soil. This holds true as to humidity, as to the heat rays, and especially as to the actinic rays of the sun. Aside from the physical factors, the psychic unrest and distrust in unacclimated persons must be considered.

Altitude.—Since it has been established [1] that shock is primarily a question of blood-pressure, altitude must be expected to play a rôle of considerable importance. Powers,[2] Freeman,[3] and others have commented on the influences of altitude, especially in instances in which the patient recently came from tide-water.

Time of Day.—There is a marked diurnal variation in the processes of metabolism of the body, beginning on waking in the morning and culminating in the evening, which is then followed by sleep and restoration. The best-fortified point is the rising tide of the morning—the vital processes then are more active, the reserve forces are at a maximum, the psychic factor at a minimum. Then, too, an entire day is available for the circulatory struggle following the operation or injury, giving a better opportunity for sleep the following night. The most unfavorable time is from 1 to 2 A. M. Night accidents are likely to be more grave than equally severe ones occurring during the day. In lingering illnesses more deaths occur in the night, especially after midnight, than during the day. How often a patient, struggling against deep shock through the night, brightens with the dawn!

Season.—Not only is there a diurnal cycle of physiologic action but there is one for the seasons as well. The end of winter and the beginning of spring finds the metabolic processes at their ebb. Injuries and operations in the midst of summer's heat are not quite so well borne. The autumn, early winter, late spring, and early summer are, generally speaking, the more favorable periods.

Temperament.—In the sanguine or nervous temperament shock is more easily produced than in the lymphatic; and in the keenly perceptive and highly imaginative, than in the matter-of-fact.

Occupation.—Professional and business men as a class are distinctly more susceptible to shock than the farmer, the mechanic, and the laborer; the sedentary, than the active; those leading an outdoor life, than those closely confined. Seafaring life usually presents hardy subjects. The industrious are better subjects than the idle. Among the criminal class the resistance to injury and operation often is remarkable and amounts to a stigma. Soldiers and sailors, on account of regular lives and exercise, are usually good surgical risks, while athletes, on account of the excessive development of the cardio-vascular system, from the physical as well as the psychic standpoint, are not so good. The worst risk is probably that of an overworked surgeon above fifty years of age.

Cachexia.—Among the most potent predisposing causes of shock are the well-known but in no wise understood metabolic phenomena appearing in the later stages of malignant tumors. The vital impairment in this class of patients is difficult to estimate correctly, and is perhaps the most unyielding of the predisposing causes, and strikes at the very foundation of vital existence itself. Cachectic patients bear operations poorly.

Hemorrhage and Anemia.—In pernicious anemia the operative risks are especially great. In chronic anemia from causes other than hemorrhage the risk is better, but is still great. In chronic anemia due to repeated hemorrhages or slow loss of blood the risk is better. In acute anemia from hemorrhage the risk is still better.

Exciting Causes of Shock.—The exciting causes of shock may be divided into psychic, chemical, thermal, toxic, and mechanical.

Psychic Causes.—Psychic or nervous shock is a well-known phenomenon and is due to the powerful impulses from the highly specialized centers of the cerebrum acting upon the vital centers of the medulla. Fear and sorrow may in themselves produce acute shock, and in occasional instances have caused death. Physiologists have called attention to these powerful influences. It would seem that impulses from this direction produce results analogous to surgical shock caused by mechanical injury. It would be indeed difficult to differentiate between prostration by fear and prostration by injury. In the majority of injuries the psychic factor is mingled with the mechanical. The deep impression left upon the brain by a powerful nervous shock often endures for months and years. The impression, however, upon the cardiac and respiratory centers rarely endures so long.

Chemical Causes.—Irritating chemicals, such as caustics and irritants of all kinds, coming in contact with the tissues, causing partial or complete destruction, or marked irritation at the point of contact, may produce shock. Experiments in which croton oil was introduced into the peritoneal cavity rapidly produced shock. This division of the subject, however, is of comparatively small practical importance.

Thermal.—The intense irritation of heat upon the nerve-endings causes powerful afferent impulses which greatly influence the centers in the medulla. Mummery[5] has pointed out that burns of the first and second degree are apt to cause more shock than burns of the third and fourth degree, because in the former the tissues undergo extreme irritation, while in the latter they are destroyed. The peculiar shock-producing quality of burns is probably due not alone to the intensity of the impulse itself but also to the fact that all the nerve-endings over a given area are included. Burns extending over more than one-half of the body very frequently cause death from shock.

Toxic Causes.—Some of the most important instances of shock are due to the combined effect of intense irritation of the nerve-endings and the constitutional disturbance. An abscess breaking into the peritoneal cavity, a viscus perforated, pouring out intensely irritating chemical compounds into the peritoneal cavity, causes numerous impulses comparable to the effect of roughly manipulating the peritoneum, or of burning the skin.

Mechanical Causes.—The most important factor in the production of shock is the mechanical. By this is meant what in physiologic parlance is described as mechanical stimulation of nerve tissue. The effect of subjecting nerve tissue to trauma is that of sending afferent impulses toward the centers. It is well known that these impulses differ in their intensity. The cumulative effect of mechanical stimulation, then, is determined by the number and intensity of the stimulations, hence the number and intensity of the afferent impulses.

It follows that the whole problem of the etiology of shock is the problem of the various kinds of stimulation of the nervous system; all other tissue may be omitted. The various tissues and organs have a susceptibility to shock in proportion to the quality and quantity of their nerve-supply. As to the quality, one would have in mind the highly specialized nerves of the testicle, of the peritoneum, the inhibitory nerves of the vagus and the superior laryngeal, the extreme sensibility of the brain, the spinal cord, and the nerve-trunks. From the quantitative point of view, a tissue sparsely supplied with nerves would naturally be less susceptible to shock. It is known that the tip of the index-finger is supplied twenty times more highly with nerve-endings than the skin in the dorsal region. It should follow, then, that a given injury of the skin of the latter region should be only one-twentieth as shock-producing as a like injury to the palmar aspect of the tip of the forefinger. In comparing the regions supplied by common sensation, the shock-producing susceptibility is then reduced to a mathematic consideration of the number of nerve-elements exposed. It is well known that crushes of the foot produce less shock than similar injuries of the hand. Cutting, tearing, or crushing of the skin causes a temporary rise in blood-pressure, which soon returns to, or sinks below, the previous level. The skin over the testicle is frequently an exception, and in this location a fall in blood-pressure may occur. It is interesting, too, to note the fall in the blood-pressure while incising the skin over the abdomen.

Neither from the experimental nor the clinical standpoint has it been demonstrated that there is an effect of any considerable importance from mechanical or thermal injury of connective tissue, fascia, tendons, ligaments, cartilage, etc. This is readily explained by the relatively small nerve-supply of these tissues. The shock-producing susceptibility of muscles is less than that of the skin, though distinctly more than that of the connective tissue, fascia, tendons, ligaments, etc.

Pathologic Physiology of Surgical Shock.—An abnormally low blood-pressure is the essential phenomenon of the state commonly designated surgical shock. There are many other physiologic changes accompanying shock, but these may for practical purposes be regarded either as results of the low blood-pressure or as factors of minor importance. Among these secondary factors or results are alteration in respiration and cardiac action, modified mental state, loss of power of both the voluntary and the involuntary muscular systems, diminution of the secretion of urine, and lowering of the body temperature. So long as the blood-pressure and circulation are sufficient for normal physiologic purposes, a

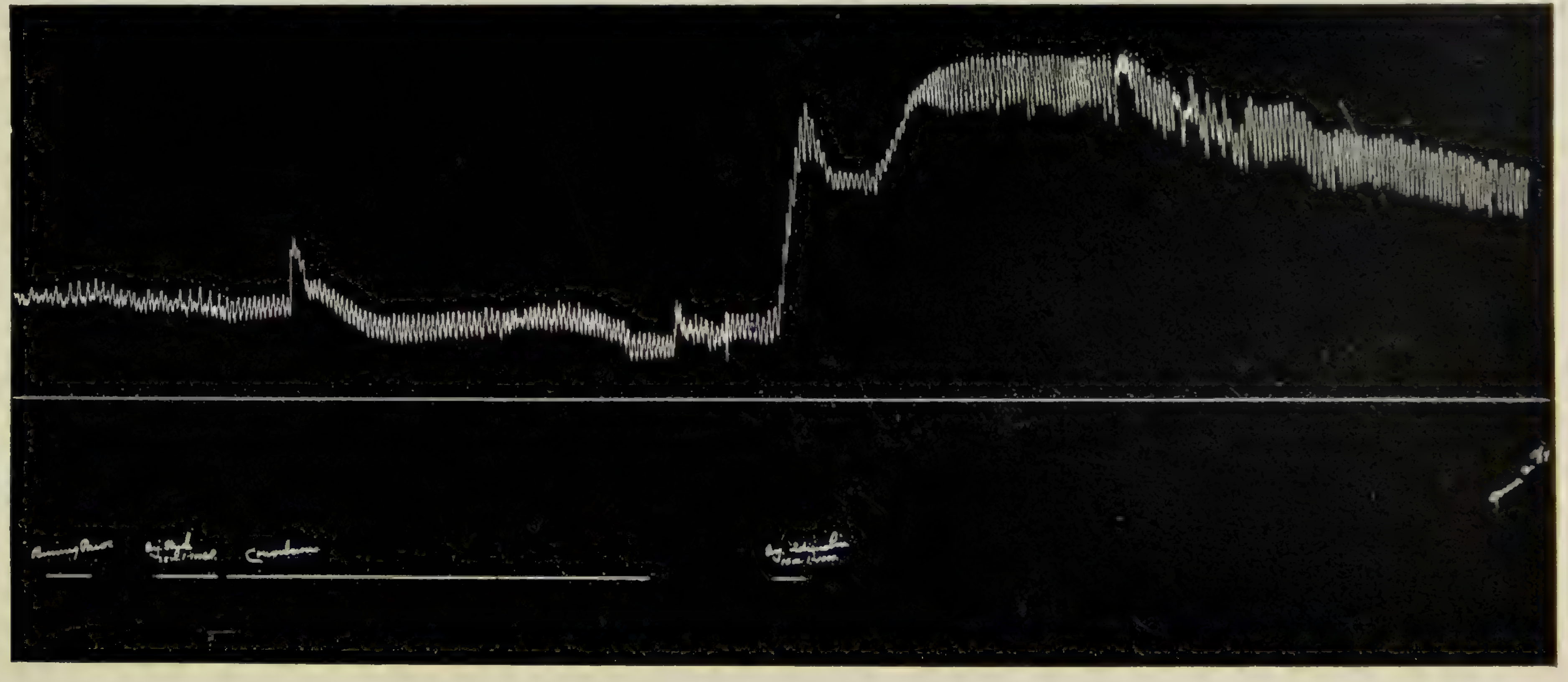

Fig. 248.—Profound Shock.

Burning of the paw caused no change in the blood-pressure. Even a therapeutic dose of strychnin caused no rise. The abrupt rise noted was due to a short convulsion. The blood-pressure was then raised abruptly higher than the normal by the injection of adrenalin. The heart was able to at once assume this burden of work, showing that it was neither paralyzed nor exhausted. This is at the same time proof that the vessel walls are active in response to stimulation.

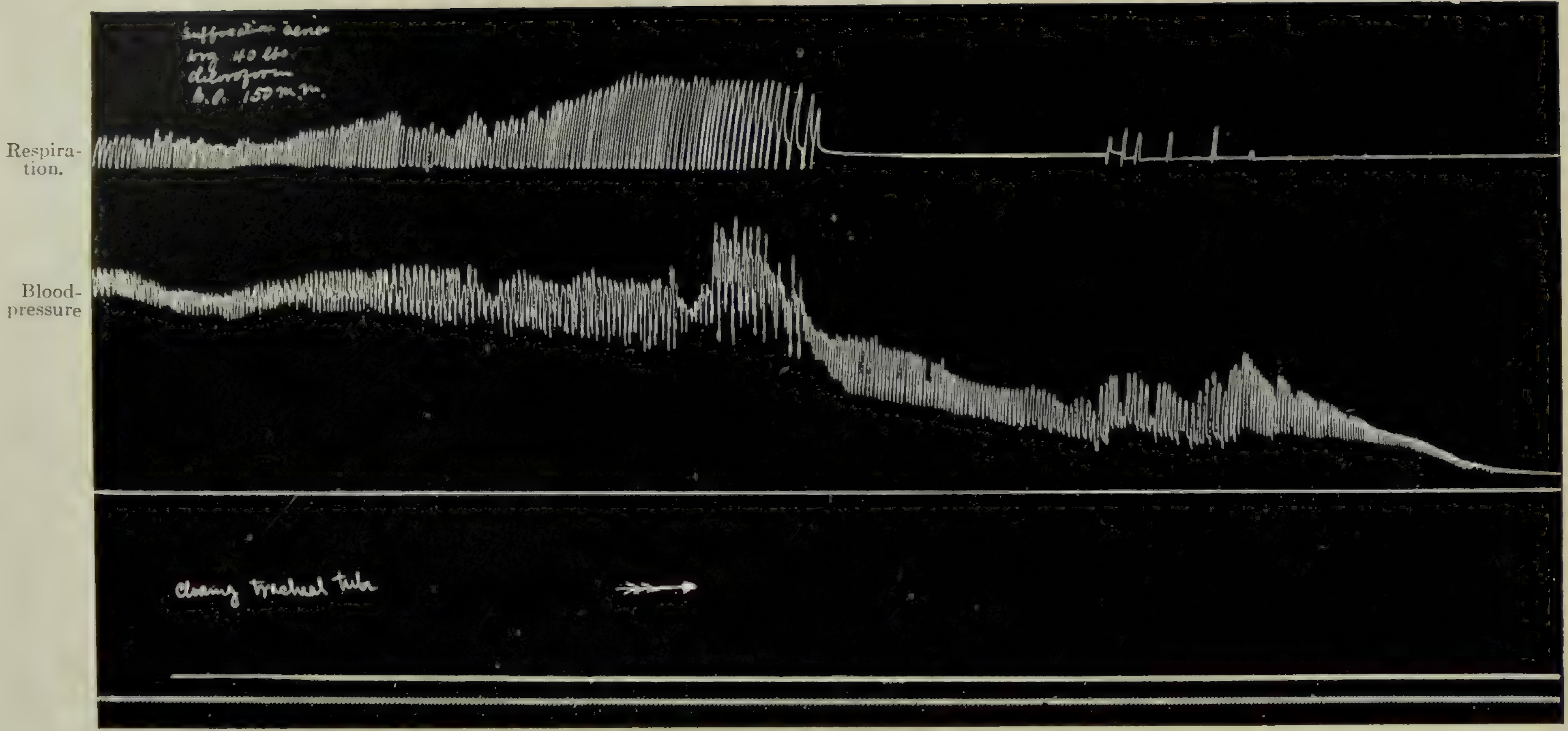

FIG. 249.—DEATH BY ASPHYXIA.

Note the temporary rise in the blood-pressure after the trachea was clamped. Note also the gradual increase in the respiratory excursions. Finally the respirations cease, the heart beats more slowly, and the blood-pressure sinks to the abscissa. Asphyxia is alway attended by a slowed pulse, and slow and powerful respiratory efforts.

serious state of shock, despite the presence of any other phenomena, cannot be presumed. As Mummery[5] has pointed out, the fall in temperature in shock is largely a result and not the cause of the low blood-pressure. The exact physical state of the vasomotor center during the existence of shock has not as yet been satisfactorily demonstrated. The result of that physical state is an inactivity of the center or centers—producing the low blood-pressure. This state of inactivity may be designated paralysis or exhaustion. But it is not certain that we can at present state just what that exhaustion or paralysis is. In a certain sense the vasomotor center in a state of shock may be designated as paralyzed, or in a certain other sense, as exhausted. We do know, however, that whatever the exact physical state is, one may conclude from the physiologic test of complete recovery that the centers are not physically damaged—that the impairment or breakdown is functional and temporary. It is at once apparent that in the management of operations prevention is more important than treatment.

Circulation.—In cases of profound shock we are warranted in concluding that the bulk of the blood does not freely circulate through the arterial system, that a large portion accumulates in the venous trunks. This state, then, would be equivalent to an intravenous hemorrhage; that is to say, the arterial system bleeds into the dilated venous system. The symptoms, then, should closely mimic those of hemorrhage. Would it be possible to differentiate between a concealed hemorrhage and shock in a case in which there was neither history nor physical signs? Most clinicians, I think, concede that such differentiation is impossible (Fig. 248).

The most important symptoms of shock are those produced by an acute anemia. The blood-pressure, as before stated, is lowered. After the carotid pressure has reached 20 mm. of mercury an irrecoverable degree may be presumed to have been reached. The pulse at first is usually accelerated, though occasionally slowed. Sooner or later it becomes rapid until the last moments of life, when it may again become slowed. The pulse-wave is short, easily compressible, and rarely dicrotic (Fig. 249).

With the progressive deepening of shock, the output of the heart with each beat is diminished, and with it there is diminution of the force of its beat. As a result of the failing circulation the face is usually blanched, though sometimes the superficial veins contain considerable blood. The gravitation of the blood into the more dependent parts of the body may be noted. The pallor noted in the face is seen in the deeper parts of the body, such as the muscles, the abdominal and thoracic viscera. Indeed, in making a dissection directly after death from shock one is at a loss to account for the normal volume of blood. If, however, just prior to death from shock, and when all the parts seem so anemic, a large dose of adrenalin be given, the volume of blood is promptly picked up and thrown into the arterial circulation, again flooding the tissues with blood.

Respiration.—Respirations are, as a rule, accelerated, sometimes sighing, irregular, and in more profound stages, rhythmic waves of increased action may appear. The respiratory changes present no characteristic symptoms. Air hunger is possibly not so marked as in cases of pure hemorrhage. The entire respiratory wave is shortened. Both the inspiratory and the expiratory phases are quickened and the pause is lengthened. In grave cases the appearance of the gasping type of respiration, with tracheal and chin tug, indicates impending dissolution.

Muscular System.—Both the voluntary and the involuntary muscular systems are relaxed: the patient maintains the posture in which he falls; the reflexes are diminished and in most profound cases the voluntary muscular power is lost.

Excretion and Secretion.—The functions of the digestive tract and the kidneys are diminished. The appearance of perspiration, even in drops, is probably due to the relaxation of the skin.

Cerebrospinal.—Cerebration is usually diminished, though the patient may be talkative and excitable. Thought is usually not consecutive. In a word, in shock virtually all the vital functions are impaired. In a given case of profound shock the symptomatology may be expressed as follows:

Facial Expression.—The face appears shrunken, pinched, and elongated, from the drooping chin, and there is a remarkable languor in the expression. The nose is small and shriveled; the tip of it occasionally presents a dusky color, making a singular contrast to the rest of the face. The eyes have lost their luster, and in the highest stages, as Mueller remarks, lie rolled up in the deeply sunken sockets, surrounded by a dusky ring. The lids are half closed, giving the eyes, as Senn[6] describes it, a seemingly staring expression. The pupils present nothing constant or special, though in most instances they are contracted. Neudorfer speaks of the eyes as if being accommodated for distance. Their reaction to light is marked. The lips are parted, thin, and usually pale. Occasionally they are cyanotic, in contradistinction to the pallor of all external mucous surfaces. The anemia and the muscular and tegumentary relaxation account for the pallor and the pinched and collapsed appearance of the face. From the loss of innervation of the masseter muscle there results dropping of the lower jaw, the partly opened mouth, the elongated face, and the partial falling in of the cheeks, the latter having lost their natural support (the teeth) and also the natural tonicity of the buccinator muscle. The sunken appearance of the eye is a result of the relaxation of the ocular muscles, especially the superior oblique; also of the empty condition of the vascular system of the orbit. The dusky coloration around the eye can be explained by the venous and capillary stagnation. This, as well as the sunken condition of the eye, is largely an individual factor, and therefore only occasionally found. The drooping of the eyelid, too, is caused by the loss of muscular tonicity; the lusterless color by the diminished lacrymal secretion and the functional disability of the eyelid.

Skin.—The general characteristics of the integument in shock—the pallor, relaxation, perspiration, etc.—which in the more severe types become apparent even to the casual observer, have met with a variety of descriptive terms at the hands of numerous writers. Jordon[7] says that the pallor of the skin has a singular white hue which only the bloodless skin is capable of presenting. The fingers and nails exhibit a bluish color and are shrunken so that the skin on the palmar aspect lies in loose folds. The cold, clammy perspiration of shock is especially found in cases due to psychic causes and in those in whom the injury occurred while engaged in bodily exertion.

Prevention of Shock.—In considering the prevention of shock we shall assume that pure surgical shock is mainly due to the effect upon the vasomotor centers of the afferent impulses set up by trauma, exposure, etc., that each such impulse modifies the functions of these centers; that a sufficient number of such impulses with sufficient intensity over a given period of time causes the vasomotor centers to lose their excitability; that during the production of this functional impairment and final breakdown the blood-pressure becomes irregular, becoming proportionately lower, and when the final stage of complete loss of excitability of the vasomotor center has been reached the pulse in the peripheral arteries cannot be palpated and the carotid pressure would probably register not more than 20 mm. mercury. This would present a picture of complete shock, with a grave prognosis.

The predisposing causes of shock may be reduced to a physiologic basis as follows: The vasomotor centers have a normal definite range of functional capacity. When one or more of these accessory factors enter, this range of definite functional capacity is by so much definitely reduced. This is a plain physiologic law.

In practice one finds one or more of these factors in the majority of his patients. That is to say, most patients are handicapped in various degrees, from the slight to the grave, even fatal. These handicaps should be our especial consideration, and our ability to estimate correctly the vital cost to execute a given technic is perhaps one of the most difficult surgical problems.

Operations upon the Head.—Horsley[8] and Spencer long ago pointed out the dangers of increased intracranial pressure, and Cushing[9] has offered an explanation of the physiologic necessity for the increased general blood-pressure under this condition.

In tumors, abscesses, and hemorrhages, causing an increased intracranial pressure, the blood-pressure of the extracranial portion is increased. This is more especially noted in the veins. The blood-pressure of the brain under these circumstances is at an irreducible minimum. Therefore, until compression of the brain has been effected it would be unsafe to lower the intracranial tension materially either by hemorrhage, anesthesia, or trauma. After having lost one case by severe, acute hemorrhage during the second stage of anesthesia, I have in severe cases opened the skull under local anesthesia.

In other instances I have detailed an assistant to make artificial respiration while the bone is rapidly cut away. Alternating heat and cold are perhaps the most powerful respiratory excitants. In two instances respiratory arrest was successfully met in this manner.

The most severe cases were those of traumatic origin, in which opportunity for physiologic compensation was greater. Marked assistance in control of the troublesome venous hemorrhage was obtained by applying the pneumatic rubber suit, and placing the patient in the 45-degree upright posture, thereby gaining the advantage of gravity in decreasing the venous pressure in the vessels of the head and maintaining, or even increasing, the arterial pressure in the same territory. In opening the skull it is very important to use the greatest gentleness if by mallet and chisel, as both the clinical and experimental evidence shows that the medulla is seriously disturbed by the repeated percussions of the mallet. In my earlier cases in opening the skull by means of the mallet and chisel, I am sure I provoked some serious circulatory disturbances. Since using only well beveled, sharp chisels more precisely and a light mallet more gently, I have not detected any circulatory changes of apparent importance.

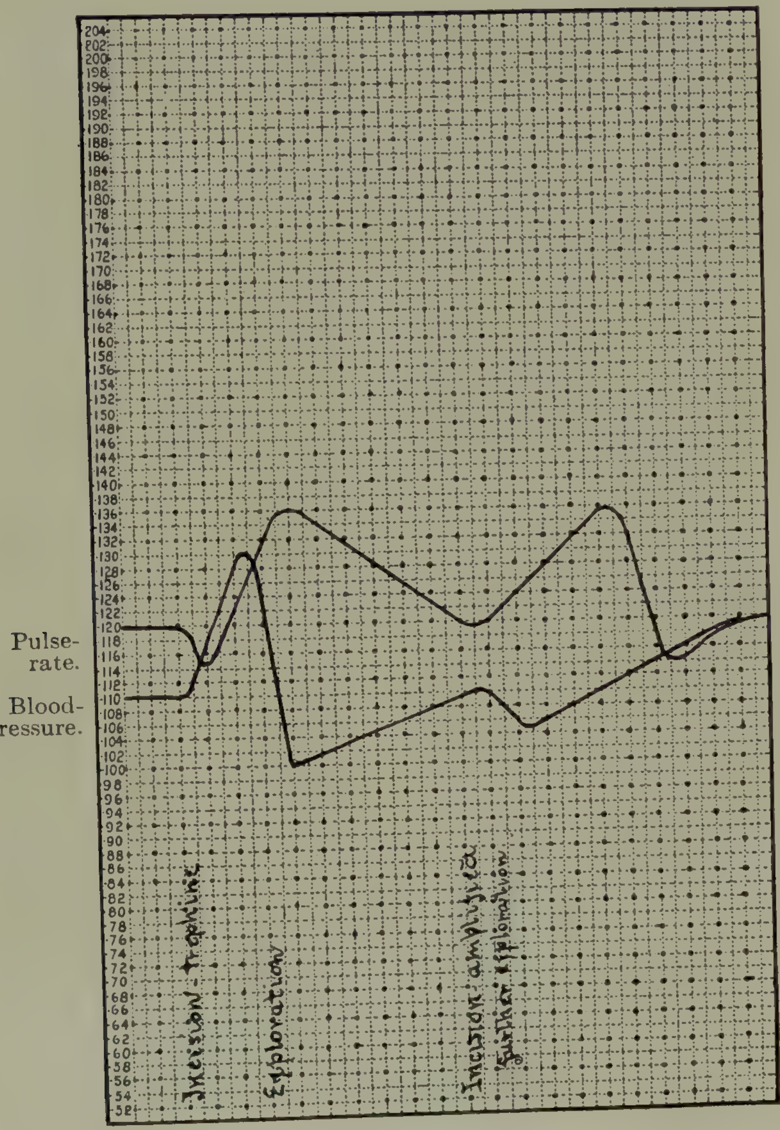

FIG. 250.—BLOOD-PRESSURE AND PULSE TRACINGS OF AN EXPLORATORY OPERATION UPON THE BRAIN.

Note the rapid rise in the pulse-rate and the fall in the blood-pressure during the manipulation of the dura and the brain.

The supreme importance of reducing to a minimum the exposure and manipulation of the meninges and the brain can only be fully appreciated by noting the circulatory changes and the loss of cortical excitability in laboratory experiments. Unless precise arrest of the hemorrhage as the operation progresses is made the operator is quite likely to do unintended damage in sponging.

Since in intracranial operations sudden circulatory disturbances are always imminent, the blood-pressure in all cases should be continuously noted by a special assistant for that purpose. The pneumatic suit is put on during the early stages of anesthesia and saline solution and adrenalin are at hand: that is to say, in the preparation for an operation the means for controlling the circulation are provided.

Laryngeal Area.—In such operations as intubations, laryngotomies, laryngectomies, intralaryngeal operations of all sorts, operators have reported instances of sudden collapse or death (Fig. 251). This is now well known to be due to reflex inhibition of the heart and of the respiration from mechanical stimulation of some part of the superior laryngeal nerve.[10]

The cardiac collapse may be wholly obviated by previously administering a physiologic dose of atropin, or by applying cocain upon the nerve-ending in the laryngeal mucosa, or by injecting its trunk with cocain. There is scarcely to be found anywhere in surgery a more definite law or a more striking phenomenon.

Among fourteen total laryngectomies performed by me for carcinoma, in the first two, before the definite cause and prevention had been worked out in the laboratory, dangerous collapse occurred; in the remaining twelve in which the superior laryngeal was cocainized not even a change in respiration or in the heart-rate was noted. Because of this dangerous reflex area in the larynx, tracheotomy is at the moment a safer operation than laryngotomy.

Thorax.—In empyema with a seriously hampered respiration and a circulation dangerously impaired one may often with greater safety do a morphin-cocain operation for a mere intercostal opening, or resection of a rib, in relieving the impending danger. After the patient's forces are recruited, a more complete operation under surgical anesthesia may be made.

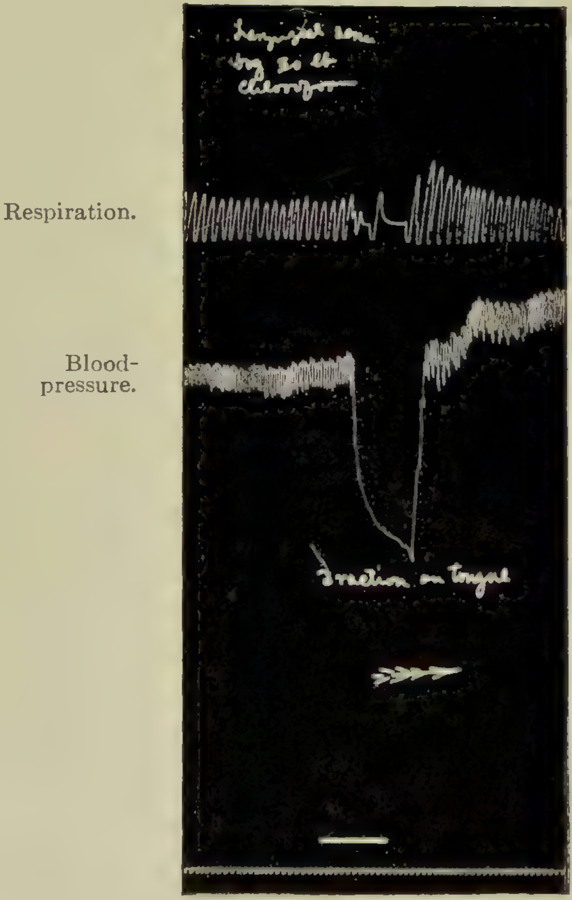

Fig. 251.

Under full ether anesthesia the tongue was drawn as far forward as possible, considerable force being used. Note the complete inhibition of both the heart and the respiration—a warning to anesthetizers.

In intrathoracic procedures one must not lose sight of the supreme importance of the respiratory action upon the circulation. This action in its assistance of the circulation has been designated the respiratory pump.

Even in the normal state the circulation is most seriously hampered when both pleural cavities are opened, thereby eliminating the suction power so necessary to fill the auricles. In such cases, while by one of the various methods of positive ventilation of the lungs, as by the Fell-

O'Dwyer apparatus, in pulmonary collapse, oxygen may be freely supplied, the greater danger, that of circulatory collapse, is little if at all obviated. Extensive pressure upon the other parts of the body is most important in throwing back the blood into the thoracic circulation and permitting the heart to refill in the face of the loss of the respiratory pump.

In all intrathoracic procedures one must ever bear in mind the high importance of not interfering with the great venous trunks; since their blood-pressure is very low, they are easily compressed. Such a compression would have an immediate disturbing value to the heart's action equal to a torrential hemorrhage.

Abdomen.—In abdominal operations the amount of shock depends in a direct ratio upon the trauma and exposure. This territory bears a rich supply of vasomotor nerves, and the effect of a given operation upon the vasomotor center is the sum of the exposure to the air and the intensity and number of mechanical contacts with the abundant nerve-supply of this territory. It follows in practice as truly as in theory that a given operation may be manifoldly more shock-producing in the hands of one operator than in those of another.

In extensive technical operations, such as the removal of tumors requiring resections of intestines, in certain cases of gastro-enterostomy, in ureteral and in all other time-consuming, exacting technics, when no special contraindication exists, morphin-ether anesthesia is used, ether and morphin during the abdominal incision, the exploration and development of the operative field, and morphin alone with slight or no other accessory during the technic proper, then ether again in closing the abdominal wound.

The region around the diaphragm and the large splanchnic trunks, as in operations for common duct stones, upon the head of the pancreas, etc., are especially shock-producing.

The expiratory moan in these upper abdominal operations near the diaphragm may deceive the anesthetizer and lead him to overanesthetize his patient. This is analogous to the inspiratory moan while working upon the sigmoid or rectum in pelvic operations, or divulsing the sphincter ani. Manipulation in the peritoneum other than the latter mentioned areas, especially if rough and extensive, may cause a powerful expulsive action, tending to force the intestines out by definite straining action. The greater the efforts at returning the intestine, the greater the mechanical stimulation, and so the greater the expulsive response, which in turn stimulates the operator to more vigorous effort, completing a physiologic vicious circle, which, when once started, continues until either the reflex or the operator is overcome. This is most likely to occur when the intestines are distended.

In anemia, cachexia, and acute infections, a most careful physiologic invoice of the available vitality should be made, and a procedure requiring an expenditure falling within such limit should be chosen. For example, in cases of acute suppurative cholecystitis, causing profound toxemia, by a cocain-morphin anesthesia a simple opening to provide drainage may be made. After the acute stage has passed, under gas or gas and ether, better drainage may be provided or further indicated measures may be executed.

The same plan may be advantageously employed in pelvic and appendiceal abscesses. That is to say, operative treatment by a process of physiologic progression is not infrequently necessary.

In operations on the pelvic organs we are impressed with the fact that this area is somewhat less shock-producing than equally extensive dissections above the pelvis.

Extremities.—The prevention of shock in operations upon the extremities has resolved itself into three simple propositions—the minimum loss of blood, the minimum manipulation and force, and the "blocking" of the nerve-trunks by intraneural injections of 10 or 15 minims of a 2 per cent. solution of cocain and eucain.

In considering the first proposition, surgeons will succeed by individual methods. For some time I have adopted the plan of direct dissection, using for the soft parts precisely the same instruments as for a breast amputation. The smaller vessels are secured in passing and a dry field is maintained. The large nerve-trunks are exposed as early as possible and "blocked." The larger vessels are ligated and divided as they are reached. Great care is exercised in so dividing the tissues that no further revision is required. The bone is divided by means of a Gigli saw, obviating the heavy manipulation of retraction of the entire stump when a plain saw is used.

As an example, in interscapulo-humeral amputations by first exposing the subclavian artery and vein and the brachial plexus through the same incision each trunk of the plexus is "blocked"; the artery and vein are then secured and the skin incision of the part supplied by the cervical nerves is made. The anesthetic may now be withdrawn, as the major field remaining has been anesthetized and rendered immune from shock by the physiologic "blocking" of the brachial plexus. As no impulses of any kind can pass either upward or downward there is no more shock in dividing the tissues, even the nerve-trunks thus "blocked," than in dividing the sleeve of the patient's coat.

Wainwright[11] has recently added important evidence of the value of spinal anesthesia in the prevention of shock in amputations of the lower extremities, from both the clinical and the experimental standpoint.

Blood-pressure observations by means of a sphygmomanometer during such operations entirely substantiate this statement (Fig. 252). However, after the effect of the "block" wears away, impulses then pass up from the injured nerves, just as after amputation by any other method, but the vasomotor centers have been protected against their greatest dangers and can better tide over the crisis.

Summary.—Every tissue and organ has a more or less individual shock-producing value and must be individually considered. The amount of shock produced by a given trauma varies according to the quantity and the special quality of the nerve-supply of the tissue involved and the number and intensity of the afferent impulses originated by the injury or operation.

Cocain or eucain may wholly "block" these shock-producing impulses. When one or more of the accessory causes of shock are present the highest possible tax is laid upon the surgical judgment of the operator. A precise technic offering a minimum of exposure and trauma, and a comprehensive grasp of all the factors entering into the operative consideration, are the ideals for which we must strive in the prevention of shock.

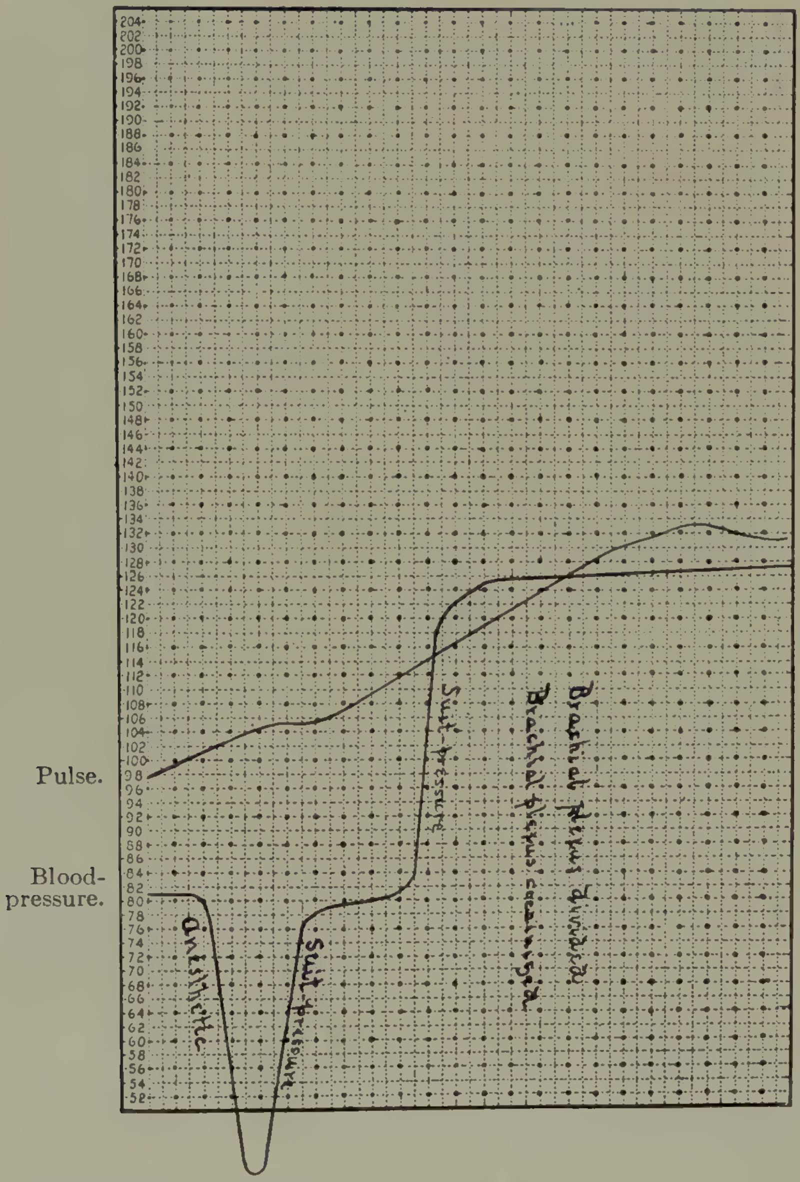

FIG. 252.—CHART OF THE CIRCULATION IN AN AMPUTATION OF THE ARM AT THE SHOULDER-JOINT ON ACCOUNT OF COMPLETE CRUSHING IN A RAILWAY ACCIDENT.

Note the rapid fall (collapse) in the blood-pressure during anesthesia. The pneumatic suit was then inflated, causing an immediate recovery and a much higher rise. The brachial plexus was carefully "blocked" by injecting the nerve-trunks with cocain before dividing. The division of the nerve-trunks did not cause the slightest change in the circulation.

Clinical Picture of Shock.—The symptoms of a patient in shock, as resulting, for instance, from a severe injury of the extremities in which the blood loss may be inconsequential, may be stated as follows: The patient lies quietly and indifferently upon his back, and in severe cases he may remain in the position in which he has been placed by bystanders. The face is pale, sometimes slightly cyanotic, elongated, shrunken, pinched, and devoid of movements. The eyes are shrunken, either staring or half closed, the cornea is lusterless, the pupils dilated and reacting but torpidly to light. The lips are thin and slightly separated; the natural redness is absent. The extremities are cold. The muscular movements may not be abolished but are markedly diminished. Only occasionally is a feeble movement attempted, or a groan, weak and hoarse, interrupts his deathlike silence. The reflexes still persist but are greatly diminished. The general skin surface is pale, but at the peripheral parts, such as the fingers and toes, there is sometimes slight cyanosis, and cold, clammy sweat—most marked on the forehead—transudes from the pores. The respiration is superficial, shallow, and irregular, frequently interrupted by a sighing expiration. The temperature may show a decrease of from one to two (seldom more than three) degrees Fahrenheit. The pulse is weak, perhaps imperceptible at the wrist. Its frequency is usually increased, though occasionally it may be decreased. The sensibility and all the special senses are impaired. The patient is apathetic and gives the impression of utter indifference to his surroundings and his own condition. He fails to respond to commands or entreaties to move or to answer questions addressed to him. The mental stupor is only too apparent. In severe cases unconsciousness completes the picture of this pseudo-death. The sphincters fail to functionate; incontinence of the feces is a frequent occurrence, that of the urine more seldom. Nausea, vomiting, and singultus may be present. Deglutition is usually difficult.

The general functional disturbance after a period of rest may disappear. The disturbance of the pulse, the respiration, the temperature, the motility, and the sensibility pass away and the approach to the normal physiologic state may be progressive. In many instances, however, "the repose needed for repair" or the appropriate treatment administered is ineffective. The general state remains unaltered; the pulse becomes imperceptible and is finally altogether lost. "This momentary pause in the act of death is soon followed by the grim reality." The autopsy offers no solution to the surgical problem.

Discussion.—The explanations generally advanced for the tegumentary disturbances are centered around the anemic condition and the relaxation of the parts. Pallor and coldness both explain themselves by the less vascular state of the skin and the retarded circulation. Coldness of the extremities is also in accordance with the disturbance of the circulation of the peripheral parts. Cyanosis or bluish discoloration is sometimes noted in the fingers, lips, and nose, and is probably found more frequently in individuals in whom cardiac, pulmonary, and other affections predispose toward a deficient oxidation and stagnation of the blood. The general relaxation of the skin finds its explanation partly in its more bloodless condition than in the normal, but more particularly in the loss of innervation of the involuntary muscular fibers, especially the ones around the hair-follicles and tegumentary glands. This relaxation, which in marked cases becomes evident at the finger-tips and especially in the face, by the formation of folds, is probably dependent to a greater or less degree upon the individual. In old persons and those debilitated by wasting disease it becomes more apparent than in the young and robust.

Relaxation of the skin also accounts for the presence of perspiration. According to Jordon, it is most likely due to relaxation of the orifice of the ducts from the diminished vascular supply and the impaired contraction of the smooth muscular fibers of the skin, which permits the perspiration to escape upon the free surfaces. It is impossible that the perspiration is secreted at the time the system is suffering from shock, because of the diminished circulation in the glands and the generally diminished activity of the secreting cells during the condition of shock.

Treatment of Shock.—In the management of shock three fundamental principles should be recognized: (1) The prevention of further shock; (2) the support of the circulation; (3) the securing of physiologic rest.

The Prevention of Further Shock.—Little need be said upon this subject in addition to the previous discussion of it. It is obvious that the importance attaching to this proposition obtains principally in cases of traumatic shock. Extensive wounds, burns, compound fractures, crushed limbs, etc., should be handled with the utmost gentleness, both on account of the psychic effect of pain, and on account of the production of dangerous shock-producing afferent impulses which attend any manipulation of tissues having a nerve-supply. It is well to emphasize the fact that although the patient is under an anesthetic, the shock-producing effect of manipulation and trauma is still great. Whenever possible large nerve-trunks should be blocked with cocain injection, provided this can be done without too much delay and manipulation. Scarcely any cases in surgical practice demand so much gentleness and precision as the management of mangled limbs.

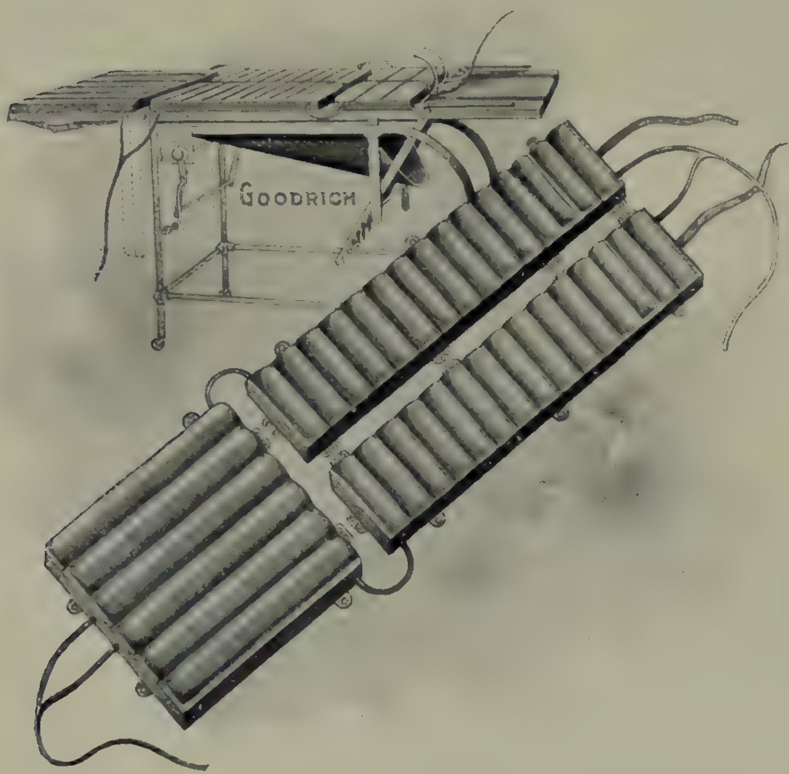

Fig. 253.—Water Pad.

Designed to allow hot water to be continuously replenished. Of value in maintaining patient's temperature while on operating table or in treatment of shock or collapse.

The Support of the Circulation.—While on the foregoing proposition there may be but little difference of opinion among surgeons, on the next surgical practice is at the present time somewhat divided. In shock many surgeons give alcohol as a routine practice after severe operations; others, both before and after; while still others never give it under any circumstances. On good authority digitalis and strychnin, and ergot and nitroglycerin, are given, singly or in various combinations. In France ergotin is frequently given; in Germany, strychnin.

The methods of supporting the blood-pressure may be classified as therapeutic and mechanical. The value of certain therapeutic stimulants, such as strychnin, digitalis, alcohol, nitroglycerin, caffein, camphor, ammonia, etc., has been subjected recently to inquiry, giving rise to considerable doubt as to their efficacy.[12] Mummery[13] has stated the more advanced position in his allusion to the use of strychnin as follows: "The administration of strychnin in shock is like beating a dying horse; it may call forth an effort if we beat hard enough, but it hastens the end." It is quite probable that the so-called heavy stimulation has done much harm.

By the use of adrenalin the blood-pressure may be raised through its action upon the vessels themselves while not modifying the vasomotor center. Mummery[13] regards certain preparations of ergot favorably for the same reason. The shortcomings of adrenalin are obvious when it is recalled that the effect of the drug is fleeting, becoming inert on oxidation. The administration of 10 to 15 c.c. of adrenalin chlorid in 500 c.c. of saline solution, given subcutaneously, may be of benefit. There are few drugs that have much value in the support of the blood-pressure in cases of true shock.

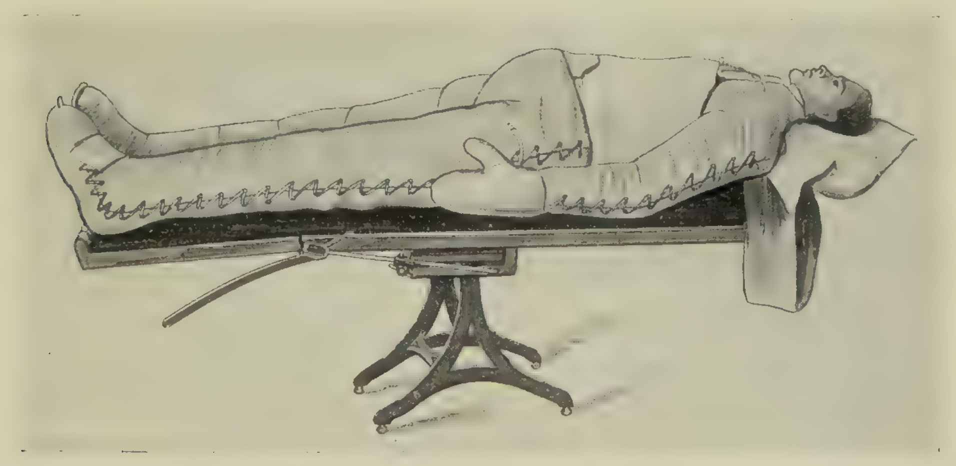

FIG. 254.—CRILE'S PNEUMATIC SUIT.

Mechanical Means.—The head-down posture, making the patient as comfortable as possible, is one of the most practical and effective methods of securing an increased determination of blood not only to the brain but to the heart and lungs as well. In addition to this, the extremities and abdomen may be bandaged. An effective plan for this consists in covering the parts to be bandaged with non-absorbent elastic cotton in heavy layers so as to permit an elastic pressure. It is not well to apply the bandage directly upon the skin, but bandaging with broad flannel bandages over heavy layers of cotton is less objectionable to the patient, obviates the risk of cutting off the blood-supply, minimizes the slipping of the bandages, retains heat, and definitely raises the blood-pressure. A similar pressure evenly distributed may be even more effectively attained by the use of the author's rubber pneumatic suit, a device made on the principle of the pleura, that is to say, a double layer of rubber which may be readily applied to the patient, laced up, and inflated with an ordinary bicycle pump. The compression has the advantage of being even, entirely under control, and may be increased or diminished without disturbing the patient. As measured by the sphygmomanometer the blood-pressure may be raised from 15 to 40 mm. mercury (Fig. 255).

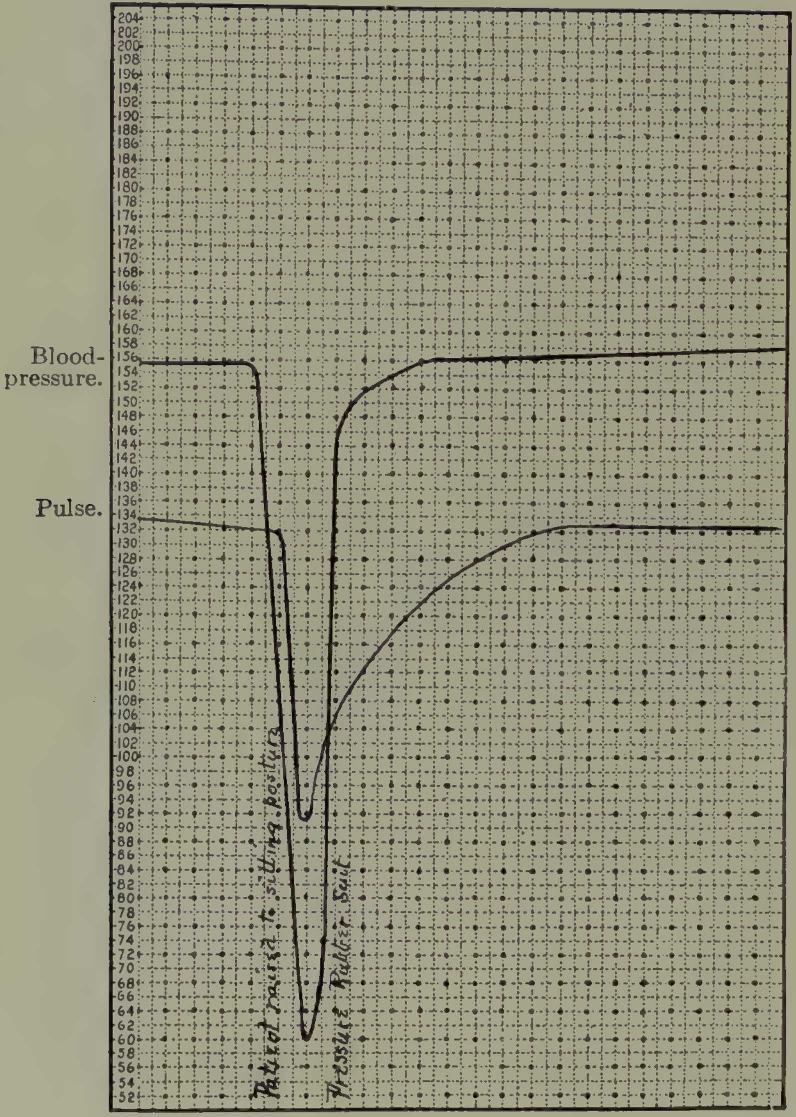

FIG. 255.—POST-OPERATIVE COLLAPSE TREATED BY INFLATING THE PNEUMATIC SUIT.

After the excision of the tongue and a "bloc" excision of the glands of the neck. The patient having been in the head-up inclined posture, was returned to his bed in good condition. The suit was then deflated. Later a venous oozing from the stump of the tongue became troublesome. When he was put upon a back-rest to overcome the venous oozing, he fainted. The pneumatic suit was then inflated, bringing immediate relief.

Another important method of mechanically supporting the circulation is by means of *saline infusions.* As Mummery[5] has pointed out, there are four principal ways in which fluids may be introduced into the circulation for the treatment of shock: First, by intravenous infusion; second by intra-abdominal infusions; third, by rectal injections; fourth, by subcutaneous injections.

In giving saline infusions it is well to bear in mind that only a certain amount will be retained in the circulation. It tends by transudation to disappear rapidly into the walls and lumen of the abdominal viscera and into the broncho-pulmonary tract. In giving intravenous infusion, any superficial vein may be selected. Great care should be taken not to permit the formation of a clot in the proximal end of the vein during the final preparation for the infusion. One of the common methods is that of exposing the median basilic vein, tying it off below, then making an incision into it large enough to accommodate the end of the canula. In emergencies a glass medicine dropper may serve as a canula. It is well to give the infusion gradually, as it has been shown by Hill and others that when the amount of fluid reaching an anemic heart is rapidly

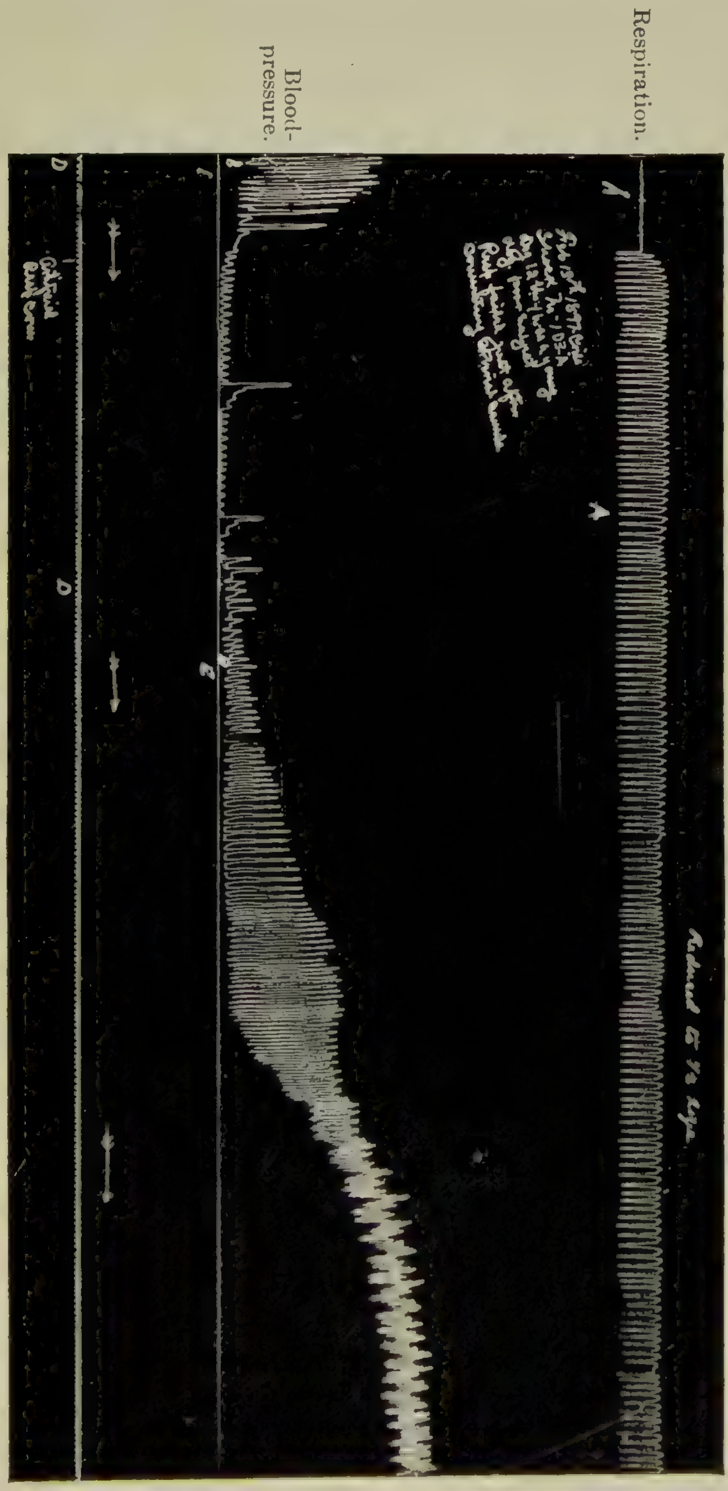

FIG. 256.—RESUSCITATION BY ARTIFICIAL RESPIRATION AND SALINE INFUSION. While preparing for an experiment the animal suddenly went into collapse. Artificial respiration and intravenous infusion of normal saline reanimated him after the lapse of 1 minute 50 seconds.

increased, acute dilatation may ensue. It is best to begin gradually, then increase the rate, and not, as a rule, give more than a pint at a time. This amount may be repeated at intervals according to indications. The temperature of the fluid should be several degrees above normal blood temperature, say 102° F., thus allowing for cooling as the fluid flows through the tube. The solution most commonly used for intravenous infusion is a sterilized normal saline solution. In collapse due to hemorrhage in the absence of shock, intravenous infusion is markedly efficacious. It supplies fluid to the circulation to replace that which has been lost. It also increases the blood-pressure in the centers, increasing their action.

Mummery[5] states that physiologic salt solution is capable of taking up oxygen in the lungs and giving it off in the tissues. In severe cases of shock the rise in the blood-pressure following saline infusion is usually not well sustained. In a short time the full pulse produced by the saline disappears (Fig. 256).

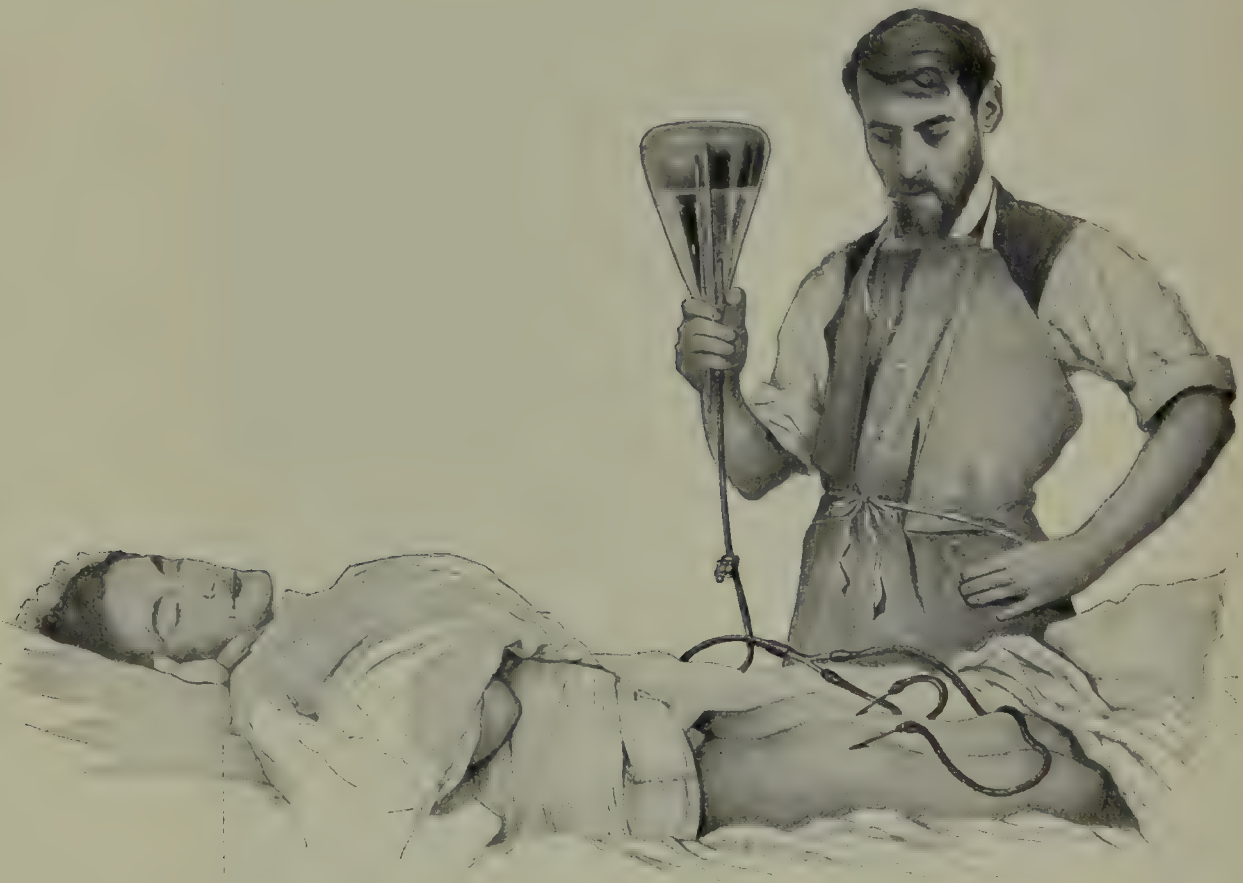

FIG. 257.—SUBCUTANEOUS INFUSION (Zuckerkandl).

Intra-abdominal Infusion of Salt Solution.—In 1887 Lawson Tait advanced the introduction of large quantities of water or saline solution into the peritoneal cavity. This practice has been in vogue in many clinics. This method is equivalent to that of the introduction of saline solution by subcutaneous infusion. In septic cases the majority of surgeons have not used it, on the ground that it diffuses the infective material. Clark has shown that flushing the peritoneum with saline solution caused a marked increase in leukocytosis, so he came to the conclusion that this method of introducing salt solution even in infections is important. The preference for this method of infusion would rest largely upon individual cases and upon the nature of the operation. It undoubtedly has an important place, as at the close of an abdominal operation attended by profound shock; when no contraindications exist, a considerable quantity of saline infusion may be administered.

Rectal Infusion of Saline Enemata.—In many instances this method has been largely practised, and it has the advantage of being readily done without inflicting pain. Murphy has recently called attention to the very gradual introduction of saline infusion into the rectum through a small catheter, the pressure being so slight as to produce a flow as slowly as the rectum absorbs it. In this manner large quantities of fluid are taken up.

Hypodermoclysis or Subcutaneous Infusion.—This method is much in vogue and seems to produce satisfactory results. Unfortunately it is painful, and one must be cautious in the asepsis and not introduce too large quantities in a given area, causing a prolonged anemia of the parts, which might terminate in sloughing. Infusion by several needles under the breasts, in the loose tissue over the pectoral muscle, in the back or thighs accompanied by gentle massage, is an effective method. This may be repeated from hour to hour or day to day as the case may require. This is especially indicated when there is not sufficient urgency to demand an immediate intravenous infusion, and when the other method of rectal infusion is not admissible or when the rectum is too irritable.

Physiologic Rest.—Not the least factor in the treatment of shock is the securing of physiologic rest. This, however, is oftentimes most difficult to attain and its best accomplishment taxes the utmost resources of the surgeon and nurse. Physiologic rest implies the calming of fears, the subduing of excitement, and the instillation of hope; it implies the relief of the important higher centers from pathologic impulses. To accomplish this, anxious and terrified friends must be controlled, the patient's surroundings must be quiet, the management precise and simple, and the surgeon in attendance must exclude from his manner every evidence of anxiety.

Summary.—(*a*) *Shock.*—Physiologic rest is the most important consideration in the treatment of shock. The patient should be kept mentally and physically at rest. Surgeons and nurses should bring assurance and confidence. The patient should be made comfortable. If this cannot be satisfactorily accomplished by management and nursing, then give a minimum of anodynes. It is not well to tax the patient with unimportant annoying routine measures. The foot of the bed should be elevated. In more critical cases the extremities and the abdomen may be snugly bandaged. Saline solution per rectum, subcutaneously or intravenously, according to the urgency, may be given.

If the foregoing seems unavailing, 15 minims of adrenalin chlorid (1:1000) may be added to 500 c.c. saline solution administered subcutaneously, and in extreme urgency a continuous infusion of 1 : 20,000 adrenalin solution at the rate of 2 c.c. per minute should be tried.

(*b*) *Collapse.*—In collapse from reflex inhibition, such as may attend

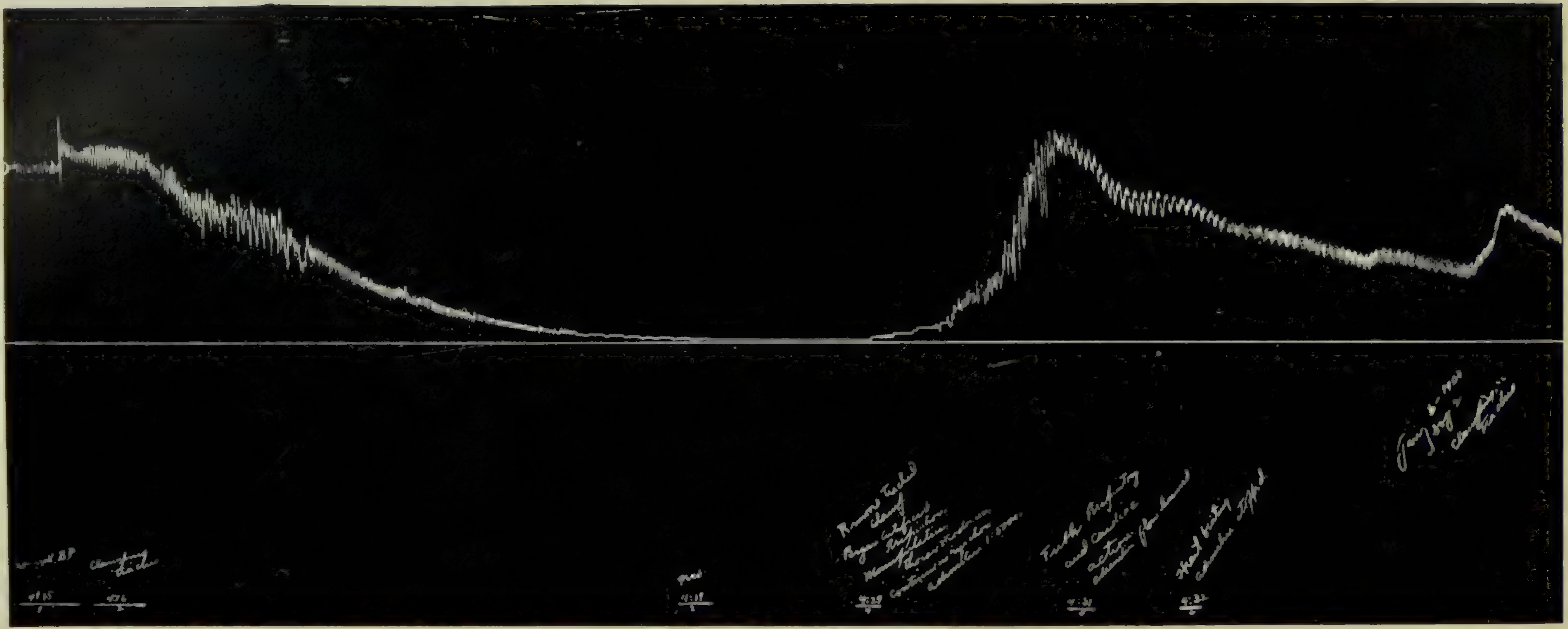

FIG. 258.—RESUSCITATION AFTER APPARENT DEATH.

The animal was killed by asphyxia. Ten minutes later resuscitation was begun by artificial respiration, rhythmic pressure upon the thorax over the heart, and the intravenous infusion of 1 : 10,000 adrenalin chlorid. Resuscitation was prompt. The animal was kept for twenty-four hours, then killed. It was able to walk, but showed no intelligence.

intubation, etc., the head-down posture with rapid, rhythmic pressure upon the thorax over the heart, thereby producing both artificial respiration, and to a certain degree artificial circulation, should be given. The heart-beat will be quickly reëstablished, and soon thereafter voluntary respiration will begin. If the collapse is due to hemorrhage, saline infusions, subcutaneously or intravenously, given according to the urgency, followed by strychnin, may suffice. The effect of strychnin is heightened by first raising the blood-pressure with saline infusion. The inclined head-down posture should be strictly maintained. In grave cases the lower extremities and the abdomen to the costal margins should be firmly bandaged over thick layers of plain cotton, or, still better, the rubber pneumatic suit may be applied. Should these measures fail, then a direct blood transfusion by making a temporary end-to-end anastomosis between an artery of a donor and a superficial vein of the patient should be tried.

After collapse from any cause has reached the stage of suspended animation, that is to say, if the circulation and the respiration have ceased, resuscitation should be attempted as follows: The patient is placed in the horizontal or head-down posture. The tongue is held well forward, and rapid, rhythmic pressure is applied upon the chest over the heart, thereby providing sufficient artificial respiration and a meager artificial circulation during the insertion of the infusion canula directed toward the heart into peripheral artery or vein. As soon as the solution begins to flow into the vessel, thrust the needle of a hypodermic syringe filled with adrenalin chlorid (1:1000) through the rubber tube near the canula, and during about one minute inject from 10 to 30 minims. In suitable cases the heart will promptly begin vigorous beating, and after some time spontaneous respiration will be established. The circulation should be closely observed, and should there be evidence of failure a continuous intravenous infusion of a 1:20,000 solution of adrenalin chlorid in normal saline solution should be given as long as required, at the rate of 2 to 3 c.c. per minute.

In the meantime the extremities and the abdomen should be firmly bandaged over plain cotton, or the rubber pneumatic suit should be applied.

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